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# and Use Committees

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# Information Resources for Institutional Animal Care and Use Committees

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## Foreward

*Information Resources for Institutional Animal Care and Use Committees* has been produced by the Animal Welfare Information Center (AWIC) of the U.S. Department of Agriculture's National Agricultural Library (NAL) in cooperation with the USDA, APHIS, Animal Care in an effort to provide a comprehensive resource for IACUC's as they conduct their routine activities, train new members, develop institutional policies and guidelines, etc.

The material in this publication has been drawn from a number of reference sources including: databases such as Medline, Agricola, TOXLINE, NTIS, CAB International; World Wide Web sites; professional organizations and Federal agencies; and publications and writings of the Animal Welfare Information Center.

The staff of the Animal Welfare Information Center hope that you find this publication to be a useful addition to your laboratory animal resources and welcome any comments for future editions.

# How To Use This Document

This publication is divided into 11 sections: Introduction to Animal Care and Use Committees; U.S. Government Principles, Regulations, Policies and Guidelines; Agency Directives for Federal Fund-holders; Professional Guidelines; World Wide Web Resources; Articles and Bibliographies; Primary References; Selected Software Providers; Organizations; Subject Index; and National Agricultural Library Document Delivery Information for U.S. and foreign patrons.

## Introduction to Animal Care and Use Committees

This article provides an overview of how the IACUC came into being under the Animal Welfare Act and its primary functions and responsibilities.

## U.S. Government Principles, Regulations, Policies and Guidelines

This section contains pertinent excerpts from the animal welfare regulations of the U.S. Department of Agriculture (USDA), selected USDA Animal Care Policies, and pertinent excerpts from the *Public Health Service Policy on Humane Care and Use of Laboratory Animals* and the *Public Health Service Guide to the Care and Use of Laboratory Animals*. Web addresses are provided for access to the full-text of these documents.

## Agency Directives for Federal Fund-holders

Institutions receiving funds or grants from Federal agencies are generally obligated to agree to abide by certain agency rules and regulations. These directives are from the National Aeronautics and Space Administration, U.S. Department of Agriculture, U.S. Department of Defense, and the U.S. Public Health Service.

## Professional Guidelines

Many professional societies have published guidelines for the care and use of animals in various disciplines. This section contains information on how to obtain those guidelines and other useful information regarding the care and use of animals in research.

## World Wide Web Resources

It's almost the year 2000, what kind of publication would we be if we didn't list websites. This section lists pertinent government web sites, clearinghouses, and selected University web pages. It is not meant to be a comprehensive listing but to get you to sites that maintain comprehensive listings. The web addresses are current as of September 3, 1999.

## Articles and Bibliographies

The primary section of this publication consists of 19 subsections broken out by various topics. Most subsections are introduced by AWIC Newsletter articles, excerpts from Federal policies, regulations, or guidelines, or information generously provided by other organizations. The reference section for each article may or may not overlap with citations in the bibliographic portion of each subsection. Immediately following the article(s) is a comprehensive bibliography containing citations that are arranged alphabetically according to the last name of the primary author. Each entry also contains descriptors and the NAL call number if the particular source is available at the National Agricultural Library (NAL). If the full-text of the article/resource is available on the WWW, the URL is provided. At the end of each subsection are listings of World Wide Web sites that will

provide additional information on the topic. Web addresses are current as of September 3, 1999.

## Primary References

This section lists useful textbooks, formularies, conference proceedings, laws, etc. that should be useful references for members of the IACUC.

## Selected Software Providers

A short listing of companies providing software to assist in the management of protocols, animal care programs, laboratory research, or to help with veterinary care.

## Organizations

There are many organizations that produce extremely useful materials for their members and other interested parties. In this section, organized by world regions, you will find information on how to contact these organizations via a variety of electronic means and that old standby, the postal service. You will also find World Wide Web addresses for those organizations that have posted homepages on the Web. However, readers are cautioned that because the WWW is a very dynamic media, these addresses may change. You will also find information on the type of organization, the resources or services offered, requestor priority, and fees (if any).

## Subject Index

The index for the publication was generated primarily from the descriptors that accompany each entry. In some instances, index words may have been taken from the title. The number associated with each index term corresponds to the *page number* on which the index term can be found.

## APPENDIX —Department of Defense Animal Use Protocol Form

The animal research protocol form that is used by research institutions of the U.S. Department of Defense.

## National Agricultural Library Document Delivery Information

The information contained here provides directions on how to obtain copies of articles mentioned in the bibliography. There are separate directions for U.S. patrons and those readers outside the United States. **All patrons are encouraged to use their local resources before contacting the National Agricultural Library.** While the National Agricultural Library provides a variety of services to patrons around the world, videocassettes are not available for loan outside the United States and Canada





# Introduction to Animal Care and Use Committees

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*The views expressed by the authors do not necessarily represent positions or policies of the U.S. Department of Agriculture or any agency thereof and should not be interpreted as such.*

## INTRODUCTION

The Animal Welfare Act (AWA) (1966) is the primary Federal law that governs the use of animals in research, testing, and teaching in the United States. Originally passed by Congress in 1966 and amended in 1970, 1976, 1985 and 1990, the AWA provides the basis for the regulatory authority given to the United States Department of Agriculture (USDA) to ensure the welfare of covered animals used in regulated activities. The Act includes all warm-blooded vertebrates, as defined by the Secretary of Agriculture, but specifically exempts all farm animals used in food or fiber research or production. Rats of the genus *Rattus*, mice of the genus *Mus*, and all birds are administratively exempted at this time by the Secretary of Agriculture. With the passage of the 1985 "Improved Standards for Laboratory Animals Act," sponsored by Senator Robert Dole and Representative George Brown, the provisions of the AWA were greatly expanded. The primary purpose of the new law was succinctly stated by Senator Dole in his remarks introducing the amendment. He said,

"Mr. President, the farm bill contains legislation dealing with the humane treatment of animals. The main thrust of the bill is to minimize pain and distress suffered by animals used for experiments and tests. In so doing, biomedical research will gain in accuracy and humanity. We owe much to laboratory animals and that debt can best be repaid by good treatment and keeping painful experiments to a minimum." (Congressional Record 1985)

The new law redefined humane care to include such factors as sanitation, ventilation, and housing. The USDA was directed to establish regulations to give dogs the opportunity for exercise and to set standards relating to a physical environment adequate to promote the psychological well-being of non-human primates. Not unexpectedly, the regulations greatly expanded the powers of the laboratory animal veterinarian and stressed the need to minimize pain and distress through adequate veterinary care and the proper use of anesthetics, analgesics, tranquilizers, and euthanasia. The principle investigator was also obligated to consider alternatives to any procedure *likely* to cause pain or distress. USDA considers alternatives in the spirit of the 3Rs of Russell and Burch (1959)--  
**R**eduction in the numbers of animals used, **R**efinement of techniques to minimize pain or distress, or **R**eplacement with non-animal techniques. To ensure that the new regulations were being followed,

the law also called for the establishment of Institutional Animal Care and Use Committees (IACUC). The IACUC was given broad powers to oversee all aspects of an institutions animal care and use program, including approval or disapproval of animal use protocols, development of training programs for animal care and use personnel, inspection of all animal areas, review of the animal care program, and investigation of any alleged problems. The development of the IACUC also allowed USDA to begin "enforced self-regulation." Under this concept, the institution is responsible for ensuring compliance with the AWA regulations and reporting any problems to USDA. To ensure that the IACUC is performing its duties, USDA inspects all research facilities at least once each year. The new law also established an information service (the Animal Welfare Information Center) at USDA's National Agricultural Library to assist both researchers and IACUCs in complying with provisions of the regulations. Finally, the law provided for severe penalties for any IACUC member that released proprietary information or other trade secrets garnered in the course of IACUC activities.

Although the AWA regulations are the only Federal regulations governing the welfare of animals in research, the *Guide for the Care and Use of Laboratory Animals* (NRC 1996) is a widely used reference on animal care and use. But, researchers receiving funding from the U.S. Public Health Service (PHS) are obligated to follow the animal care standards found in the *Guide* and must assure the PHS that they are doing so. Unlike the AWA, the *Guide* covers all species of animals used in biomedical research. By and large, the standards found in the *Guide* and the AWA regulations have been harmonized.

Because of the legal burden placed upon IACUCs, it is important to understand the organization and make-up of the committee, the regulations they are required to follow, the processes involved in review and inspection of the institution's policies and physical plant, the process of protocol review, common IACUC problems, and finally, a look at special issues in research.

## ORGANIZATION

Under the 1985 amendments, each institution must designate an Institutional Official (IO), who has the authority to legally commit on behalf of the research facility that the regulations of the AWA will be followed. The IACUC, which is appointed by the chief executive officer, reports directly to the Institutional Official. Although the IACUC is responsible for evaluating the animal care program, it is the IO who has ultimate legal responsibility for ensuring compliance with the regulations and proper functioning of the IACUC. Under both the AWA and the *Guide*, the IACUC has final authority to disapprove any activity involving the care and use of animals. However, activities approved by the IACUC may be subject to further scrutiny by the institution (USDA 1995b; NRC 1996).

## MEMBERSHIP

The AWA provides that, at a minimum, each IACUC shall be composed of the chairman, a veterinarian, and an unaffiliated member. The unaffiliated member, as the name implies, has no affiliation with the institution and can receive only minimal compensation (e.g., travel expenses, meals, or modest monetary payments for participation) from the institution. If the committee is composed of more than three members, not more than three members can be from the same administrative unit.



By contrast, the *Guide* requires that an IACUC should include a practicing scientist experienced in research involving animals, a veterinarian experienced in laboratory animal science or medicine, and one must not be affiliated with the institution. The PHS Policy also discusses committee membership. A survey of 477 research facilities in 1995 found that most IACUC's consisted of 7 members with a range from 3 to 50 members (Borkowski 1996).

### ***The Veterinarian***

The veterinarian must be trained and experienced in laboratory animal science and medicine, and must have direct or delegated responsibility for the animal care program and activities involving animals. The veterinarian should also help determine the institution's goals for its animal care program, develop training programs to ensure humane treatment of animals, and promote the use of alternatives to animals whenever possible (Van Hoosier, 1987; Schwindaman 1994).

### ***The Non-affiliated Member***

The role of the non-affiliated member (NAM) has recently been the subject of much debate in the United States. The inclusion of NAM's on animal care committees was a hard fought victory for advocates of laboratory animals (Stevens 1986). Under both the AWA and the *Guide*, the role of the NAM is to "provide representation for general community interests in the care and treatment of animals" (USDA 1995b; NRC 1996). Members of animal protection groups wanted the NAM to have a background in animal protection efforts and thought that the NAM would provide greater accountability from researchers. However, the NAM is appointed by the CEO with little input from the community and oftentimes has no background in animal welfare or animal protection. One of the reasons for this hesitancy to appoint animal protectionists is the underlying fear that s/he may be obstructive or damaging to the actions of the committee (Levin and Stephens 1995). In the industrial sector, the whole issue of the nonaffiliated member is clouded by the possibility that trade secrets or other proprietary information could be made public. However, Congress recognized this possibility and provided for serious criminal penalties for release of trade secrets by anyone on the IACUC (USDA 1995b).

Many observers agree that the NAM brings an unbiased view to the IACUC, and ensures that animal use is essential. By providing public accountability, the NAM serves as "the built-in integrity factor to counter negative public perception or prevent the real potential for conflict of interest" (Theran 1997).

## **FEDERAL REQUIREMENTS FOR IACUC ACTIVITIES**

The primary functions of an IACUC are to review and inspect all aspects of an institution's animal care and use program including all animal facilities and animal care records, review animal use protocols, review and investigate complaints about animal use, and make recommendations to the Institutional Official (USDA 1995b; NRC 1996). The purpose of these reviews and inspections is to provide a mechanism that ensures compliance with all regulations and policies and allows for interaction between the IACUC and institutional staff members. The IACUC becomes a group of individuals rather than a faceless in-house regulatory body, which serves to lessen the sometimes adversarial nature of the review process.

## ***Review of the Animal Care Program***

At least once every 6 months, the IACUC must conduct a thorough review of the institutions program for humane care and use of animals. It is useful to use the AWA regulations and the *Guide* as the basis. Evaluation of the program should concern itself with how these activities are administered, implemented, and documented. It will necessarily focus on record-keeping and review of written procedures and policies. The programs that should receive a thorough evaluation include all IACUC procedures and policies, methods for protection of personnel that report deficiencies in animal care or treatment, procedures for filing of semi-annual and annual reports to the Institutional Official and/or USDA, the facilities program of veterinary care, the occupational health program for animal care personnel, and finally, the facilities training program for all personnel involved in the use of animals (McLaughlin 1993).

## ***Facility Inspections***

As with the program review, facility inspections must be completed once every 6 months by the IACUC. By observing the animals in their daily quarters, the IACUC can most readily determine if the institutional animal care policies are promoting the welfare of the animals. Another compelling reason is that the inspection ensures that the facility is complying with all Federal regulations and guidelines.

Members of the IACUC tour the facility's animal rooms, study rooms, feed and bedding preparation areas, necropsy rooms, cage wash areas, and any other rooms used in the animal program. If animals are routinely transported to laboratories or are maintained in satellite facilities, these areas must also be inspected. In addition to examining the animals, animal care personnel should be questioned about the daily and weekly animal husbandry routine. Facilities housing dogs and non-human primates have to meet special requirements concerning the well-being of these animals. It is imperative that the IACUC pay special attention to the implementation of these requirements for exercise in dogs and environmental enrichment for non-human primates. During the inspection process, the IACUC member should take detailed notes documenting, as needed, minor and significant deficiencies, or outstanding innovations that have improved animal welfare. These notes will be used in preparation of the report to the Institutional Official.

After the program review and facility inspection, a detailed report is generated noting any significant or minor deficiencies, the probable reason for the deficiency, and plans for corrective actions including a timetable for completion of these actions. The report should also note outstanding aspects of the program and facilities. Significant deficiencies, those that pose an immediate threat to the health or safety of the animals, must be corrected within a reasonable time frame. Any failure to adhere to the plan that results in a significant deficiency remaining uncorrected must be reported to the USDA and any Federal agency that has provided funding for a project. The final report must be approved by a majority of the IACUC and must include any dissenting viewpoints.

## ***IACUC Review of Protocols***

Both the AWA and the PHS *Guide* mandate the review of animal research protocols by the animal care and use committee before any research may begin. The AWA also requires the IACUC to review all approved protocols on an annual basis. The IACUC must review and approve, require modifications to a proposal in order to secure approval, or disapprove any protocol which it receives.

The institution is given leeway in determining the most appropriate means of complying with these requirements (Dresser 1989). The regulations and guidelines do not specify the frequency of meetings for IACUC's, leaving this to the needs of each institution. Animal care committees at large institutions may meet every week while smaller institutions may be able to function with bimonthly meetings.

The AWA mandates very specific criteria that must be met before an IACUC may grant approval to new proposals or changes in existing protocols (Schwindaman 1994; USDA 1995b). Those criteria include:

- ★ procedures involving animals will avoid or minimize pain or distress to the animals;
- ★ an investigator must consider using alternatives to procedures that might cause pain or distress to animals. Further, the investigator must provide a written narrative discussing why alternatives can or cannot be used. The narrative must also include a list of the databases searched and the keywords used in the search strategy, and/or any other sources consulted;
- ★ the investigator must provide written assurance that the proposed activities are not unnecessarily duplicative;
- ★ if painful or distressful procedures are unavoidable, the procedures must: be performed with appropriate anesthesia, analgesia, or sedatives, unless withholding them can be scientifically justified; involve a veterinarian in the planning (review by a veterinarian on the IACUC after the protocol has been submitted is not acceptable; the veterinarian should be consulted before the protocol is submitted.); never use paralytics without anesthesia;
- ★ animals that experience severe or chronic pain that cannot be relieved will be euthanized at the end of the experiment or, if appropriate, during the experiment;
- ★ the animals living conditions must be appropriate for the species and must contribute to their health and comfort;
- ★ any medical care required by the animals will be provided by a qualified veterinarian, i.e. a veterinarian trained in laboratory animal medicine;
- ★ people that will be performing any procedures on animals will be qualified and trained to perform the procedures;
- ★ any procedures that involve surgery will include appropriate pre- and post-operative care. All survival surgeries must use aseptic technique including the use of sterile gloves and masks. Operative procedures that penetrate or expose a body cavity or procedures that result in permanent impairment of physical or physiological functions (major procedures) must be performed in a dedicated surgical facility that is maintained in aseptic condition. Rodents are exempted from this requirement. Minor surgical procedures must be performed aseptically but do not require a dedicated site;
- ★ use of an animal in more than one major operative procedure, from which it is allowed to recover, is prohibited unless it can be justified scientifically, is necessary for the health of the animal, or unless special permission is obtained from the U.S. Department of Agriculture;
- ★ use of professionally recognized methods of euthanasia, unless a different method can be scientifically justified. The guidelines developed by the American Veterinary Medical Association in 1993 are generally recognized as the currently accepted standard.
- ★ identification of the species to be used and the number of animals requested;
- ★ the scientific rationale for using animals, and the reasons for using the requested



- species and the number of animals;
- ★ a complete description of the procedures involving animals and;
- ★ a complete description of the methods that will be used to minimize pain and discomfort to that which is unavoidable and necessary to the collection of *scientifically* valuable data.

## THE ANIMAL USE PROTOCOL REVIEW FORM

While Federal regulations give rather specific requirements for what an IACUC must consider for approval or disapproval of animal use protocols, the actual method for collecting that information has been left to the scientific community (Dresser 1989). However, the protocol review form is the key to the entire process for it provides the IACUC members with the necessary information required for them to perform their jobs (Prentice *et al* 1991). A successful review form should be regarded as a dynamic document that can change with the institutions experiences and evolving regulatory, professional and societal standards (Prentice *et al* 1991). A well-designed review form challenges the scientist to examine and justify, both scientifically and ethically, all aspects of a procedure that affects the well-being of the animals (Russow 1995).

To assist the scientist and the members of the IACUC, each institution should develop policies or standard operating procedures on common painful experimental procedures that carry a "high ethical cost," so that everyone involved in the review process has a common point of reference and consistent decisions are rendered. This also leads to a more efficient IACUC as time is not spent resolving the same conflicts time and again. Some of these procedures would include the use of complete Freund's adjuvant, death as an endpoint, tumor burdens, food and water deprivation, and LD50 studies for both toxicology and infectious disease studies (Dresser 1987). Institutional guidelines may require that alternative methods be used for particularly painful procedures, may list criteria for euthanizing animals during a painful procedure, or may provide guidance as to monitoring animals for symptoms of pain or distress.

## THE PROTOCOL REVIEW PROCESS

Contrary to public perception, the animal care and use committee is not an animal welfare committee. If IACUCs were required to approve protocols based solely on animal welfare issues most protocols would be rejected. The primary purpose of protocol review is to promote the welfare of animals without compromising valid scientific objectives that might benefit other animals and humankind. Protocol review is a moral and ethical evaluation that necessarily requires the evaluation of the science involved (Prentice *et al* 1990; Prentice *et al* 1992). Without addressing the validity of the proposed scientific objectives and methods, the IACUC can't decide if the ethical cost weighed against the potential benefits is morally justifiable (Prentice *et al* 1992; Russow 1995). It would appear that the *Public Health Service Policy on Humane Care and Use of Laboratory Animals* (PHS 1996) provides the IACUC, as an appropriate institutional review board, with a legal basis for considering scientific merit of a proposed research activity. According to this document "procedures involving animals should be designed and performed with due consideration of their relevance to human or animal health, the advance of knowledge, or the good of society." (OPRR 1991; Prentice *et al* 1992)

The review process will be different at different institutions depending upon the needs of the facility. A committee may delegate review of protocols to a review team or may require all members

of the IACUC to review the form. Regardless of the process used, the AWA and PHS *Guide* require that all members of the committee have full access to the protocol review form. Federal regulations and guidelines allow the designated reviewers to approve, require modifications to, or disapprove a protocol. But any member of the IACUC may request full committee review. Approval by the full committee requires that a quorum be present and a majority vote to approve (USDA 1995b; NRC 1996).

Because IACUCs are asked to review a broad range of activities, many of which may be outside the expertise of the committee, the use of consultants is allowed. However, the consultants do not have voting privileges unless they are members of the IACUC.

During the review process, the members of the IACUC should carefully assess the information provided by the scientist on the animal protocol form. If for any reason a reviewer is not satisfied with the information provided by the scientist, s/he may submit questions to the scientist asking for clarification or additional information. Typical reasons for a protocol being sent back to a scientist would include:

- ★ lack of justification for the species or number of animals requested;
- ★ criteria for alleviation of pain or distress, or use of euthanasia during an experiment is inadequately addressed;
- ★ consideration of alternatives not addressed;
- ★ lack of assurance that the proposed procedure is not unnecessarily duplicative;
- ★ incomplete description of proposed activities, post-procedural care, or endpoints not clearly defined.

### ***Consideration of Alternatives***

Animal welfare regulations require that an investigator performing procedures that are painful or distressful to the animal provide assurance that no alternatives exist to the painful procedure. To provide this assurance, the investigator must provide, except in unique circumstances, a written narrative that describes the literature databases searched (e.g., Medline, EmBase, Biosis Previews, AGRICOLA, PREX), the keywords or strategy used to retrieve information, and a brief description of why alternatives are or are not available. In some circumstances, the IACUC may allow the investigator to provide other information describing the “methods and sources used to determine that no alternatives were available to the painful or distressful procedure” (DeHaven 1999). The IACUC must satisfy itself that alternatives were adequately considered and must discuss the use of alternatives during meetings and note the discussion in its minutes. These must be made available to USDA inspectors, if requested. (USDA 1989). Stokes and Jensen (1995) have developed guidelines to assist IACUCs in reviewing protocols for alternatives. Some institutions have developed animal alternatives committees (James et al 1995; Holden 1997) or appointed librarians familiar with this type of searching (Keefer and Westbrook 1996) to help the IACUC with this aspect of protocol review. Smith (1994) has written a method paper on searching for alternatives that is an overview of this type of searching.

To assist both investigators and IACUCs, the 1985 amendment to the Animal Welfare Act established the Animal Welfare Information Center (AWIC) within USDA's National Agricultural Library. AWIC provides literature searching services and produces numerous publications and workshops on animal welfare and the use of alternatives in research, testing, and teaching.

As mentioned previously, the law provides for an annual review of protocols by the IACUC. The investigator should use this review as an opportunity to reexamine the literature for alternatives that may have been developed since the prior review.

### ***Expedited Review of Animal Use Protocols***

Under the Animal Welfare Act the principal investigator is required to provide the animal care and use committee with a written description of all activities that involve the care and use of animals that are covered by the regulations. If a full committee review is not apparently necessary or is not requested, then an expedited review of the protocol may be made. For an expedited review, the committee chairman designates at least one member of the IACUC who is qualified to conduct the review to review the protocol. This designated individual(s) is to review the protocol and has the authority to: (1) approve the protocol, (2) require modifications to the protocol, or (3) request a full committee review of the protocol. If a full committee review is requested, approval may be granted only after review, at a convened meeting of a quorum of the IACUC, and with approval vote of a majority of the quorum present. No member of the IACUC may participate in a protocol review or approval, or be part of a quorum, if that member has a conflicting interest in the protocol, except to provide requested information to the IACUC. The IACUC member making the expedited review does not have the authority to disapprove a protocol. Disapproval, or suspension, of a protocol may only be done by a majority vote of a quorum at a convened meeting of the IACUC.

## **SPECIAL ISSUES**

### ***Appropriate Animal Numbers***

One of the primary responsibilities of the IACUC is to ensure that the fewest animals possible that will yield scientifically valid data are used in an experiment. Too many animals are an unethical waste of animals and an improper use of research funds. The same argument holds true for using too few animals. However, with proper planning and consultation with a biostatistician, calculating the proper number of animals can be attained. It should be noted, however, that other factors, such as ethical considerations, may also influence the number of animals in a sample size.

The scientist must provide adequate justification for the number of animals proposed for the protocol. The appropriate number of animals for a study will be determined by the variability of the parameter being studied and the statistical tests to be used in analyzing the experimental results (Festing 1992). To successfully use statistical formulas for determining sample size, the scientist must have some idea of several parameters: the probability of accepting a false positive (alpha error) or a false negative (beta error), the smallest difference worth detecting (effect size), and the variability of experimental groups (Mann et al. 1991; Festing 1995). Proper scrutiny of the relevant scientific literature may provide information on effect size and variability allowing the investigator to assign precise values to these variables for use in power analysis or other methods for estimating sample size.

Because of the profound effect of variability on the response of animals to an experimental challenge, it is necessary to understand this source of error if animal numbers are to be minimized (Festing 1992). To minimize within group variability it is imperative that animals be free of clinical or sub-clinical disease and not subject to environmental or dietary stress (except as part of a protocol). The use of inbred strains of laboratory animals will further reduce variability and the



number of animals needed because their high degree of uniformity increases the statistical power (the probability that a statistical test will detect a difference when the difference actually exists) (Festing 1995).

Erb (1996) has provided an excellent review of the actual elements of the sample size calculations, issues that determine which sample size formula to use, and methods to decrease the needed sample size when the calculated sample size is impractical to use.

### ***Minimizing Pain and Distress***

U.S. animal welfare regulations define a painful procedure as one that "would reasonably be expected to cause more than slight or momentary pain or distress in a human being to which that procedure was applied, that is, pain in excess of that caused by injections or other minor procedures" (USDA 1995b). Investigators are required to consult with a veterinarian to assure that pain or distress is minimized. Because many studies have the potential for causing pain in animals, the IACUC should establish guidelines for periodic monitoring of animals, set criteria for veterinary intervention to alleviate pain through use of analgesics or euthanasia, and require training for investigators and animal care personnel to ensure that all can recognize symptoms of pain and distress. Morton (1985) and other authors (Soma 1987; NRC 1992) provide comprehensive reviews on recognition of pain and distress in laboratory animals. The IACUC should make these available to animal use personnel.

### ***Alternatives to Death as an Endpoint***

Because certain studies may cause irreversible pain or distress before death ensues, the investigator should strive to incorporate earlier endpoints that will satisfy the requirements of the study and spare the animal a painful death (Siems and Allen 1989; Olfert 1995). Also, an earlier endpoint may result in better scientific data as the death of the animal may result in postmortem changes to tissue or body fluids (Amyx 1987a; Siems and Allen 1989). Because these earlier endpoints may be best addressed as part of the experimental design, IACUC review of the experimental design becomes very important, especially in infectious disease studies (Amyx 1987b).

Hamm (1995) has proposed guidelines for IACUC acceptance of death as an endpoint. By establishing clear guidelines or criteria for early euthanasia of animal subjects, the IACUC can clearly minimize the pain or distress that the animal will experience. Numerous authors have outlined these criteria (Morton 1985; Tomasovic 1988; Hamm 1995; Olfert 1995). Frequently mentioned variables that should be observed include body weight, physical appearance, clinical signs such as temperature, heart rate, or bleeding, unprovoked behavior of the animal, and responses to external stimuli. In infectious disease studies, the investigator should use information available from the infectious disease literature on progression of symptoms, time course of the disease and other unique features of the disease being studied to establish earlier endpoints (Soothill *et al* 1992). In some studies there may be a scientifically valid reason for allowing the progression to death. However, inconvenience to the investigator or cost of alternatives are not acceptable reasons (Tomasovic 1988).

### ***Alternatives in Antibody Production***

This has emerged as a very controversial topic in the United States. In 1997, the U.S.

Department of Agriculture and the National Institutes of Health were petitioned by the American Anti-Vivisection Society to ban the use of animals in the production of monoclonal antibodies (MAb) via the ascites method. Although several European countries have regulations limiting or prohibiting the use of animals for MAb production (McArdle 1997), at this time USDA has no statutory authority to prohibit the use of animals for MAb production.

Production of antibodies in animals usually involves the use of an adjuvant or priming agent, such as Freund's complete or incomplete adjuvant or pristane, in conjunction with a selected antigen to stimulate the immune system of an animal to produce titres of antibodies. But it should be remembered that the purpose of the adjuvant is to induce antibodies not pain (Amyx, 1987b). Both types of Freund's adjuvants are known to produce serious inflammatory reactions that may result in abscesses, granuloma's or tissue necrosis. Consequently, IACUC's should always question the use of these adjuvants and should urge investigators to use alternative adjuvants such as Montanide ISA or Ribi's. These alternative adjuvants may provide immunopotential similar to Freund's but without the severe pain associated with the use of Freund's (Hanly *et al.*, 1997).

The production of MAb's via induction of ascites fluid has been an important tool in immunological and infectious disease research. However, unless the mouse or other animal is carefully monitored, the potential for severe pain is very real. In 1974 Kohler and Milstein showed that MAb's could be produced with in vitro methods. With Niels Jerne they won the 1984 Nobel Prize for their in vivo and in vitro work on MAb production (McArdle, 1997). Current in vitro methods widely used in Europe and the United States include modular bioreactors, static and agitated suspension cultures, and membrane-based and matrix-based culture systems (Marx *et al.* 1997; Petrie 1997). Modular bioreactors used in the United States have been found to rival the efficiency of the ascites method (Petrie 1997). The use of these in vitro methods, besides eliminating the use of animals, have the added advantage of being free of contaminating antibodies, cytokines and similar biologically active materials. Because the primary purpose of the IACUC is to minimize pain in animals, it should always encourage the use of alternative methods of MAb production at both the institutional and laboratory level. To assist IACUCs, a comprehensive bibliography on adjuvants and antibody production is available at <http://www.nal.usda.gov/awic/pubs/antibody/> (Smith *et al.* 1997). Proceedings of a conference—Alternatives in Monoclonal Antibody Production—sponsored by NIH and The Johns Hopkins University Center for Alternatives to Animal Testing are available at [http://altweb.jhsph.edu/~caat/pubs/tech\\_reports/techreport08.htm](http://altweb.jhsph.edu/~caat/pubs/tech_reports/techreport08.htm)

## CONCLUDING REMARKS

The 1985 amendments to the U.S. Animal Welfare Act have had a profound effect on the way that scientific research is conducted in the United States. With the establishment of institutional animal care and use committees, scientists wishing to conduct research using animals must receive approval from a committee composed of their peers and a representative of the general public. This accountability, for the privilege of using live animals in scientific endeavors, is enforced by periodic, unannounced inspections by veterinarians from the U.S. Department of Agriculture. Although no system of oversight is without problems, the animal care and use committee process in the United States seems to be doing its job of facilitating science while allowing for the welfare of those animals that must be used in research. However, with continuing societal concern over the use of animals in research, these committees should be advocates for alternative methods that implement the 3Rs of Russell and Burch (1959) whenever possible.



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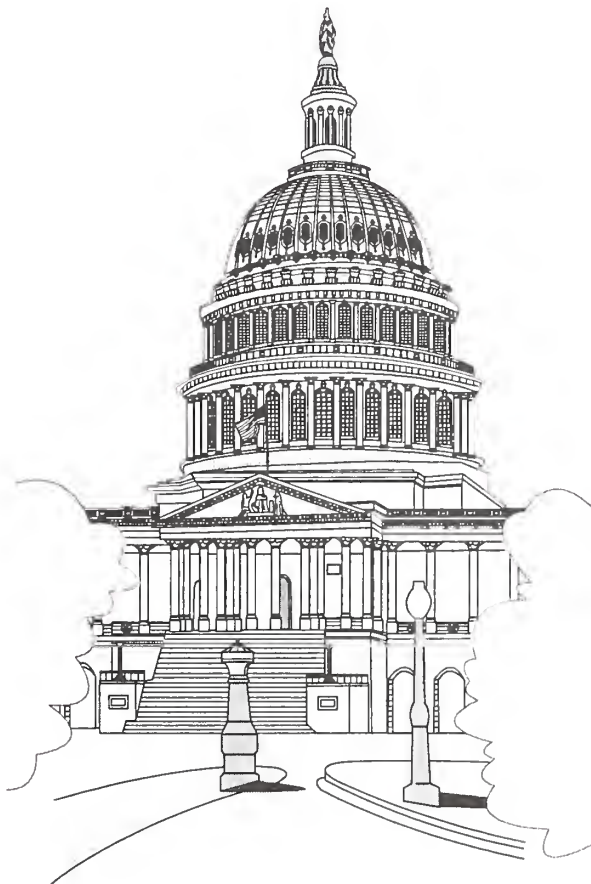
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# **U.S. Government Principles, Regulations, Policies, and Guidelines**







# **U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training**

The development of knowledge necessary for the improvement of the health and well-being of humans as well as other animals requires in vivo experimentation with a wide variety of animal species. Whenever U.S. Government agencies develop requirements for testing, research, or training procedures involving the use of vertebrate animals, the following principles shall be considered; and whenever these agencies actually perform or sponsor such procedures, the responsible Institutional Official shall ensure that these principles are adhered to:

I. The transportation, care, and use of animals should be in accordance with the Animal Welfare Act (7 U.S.C. 2131 et. seq.) and other applicable Federal laws, guidelines, and policies.

II. Procedures involving animals should be designed and performed with due consideration of their relevance to human or animal health, the advancement of knowledge, or the good of society.

III. The animals selected for a procedure should be of an appropriate species and quality and the minimum number required to obtain valid results. Methods such as mathematical models, computer simulation, and in vitro biological systems should be considered.

IV. Proper use of animals, including the avoidance or minimization of discomfort, distress, and pain when consistent with sound scientific practices, is imperative. Unless the contrary is established, investigators should consider that procedures that cause pain or distress in human beings may cause pain or distress in other animals.

V. Procedures with animals that may cause more than momentary or slight pain or distress should be performed with appropriate sedation, analgesia, or anesthesia. Surgical or other painful procedures should not be performed on unanesthetized animals paralyzed by chemical agents.

VI. Animals that would otherwise suffer severe or chronic pain or distress that cannot be relieved should be painlessly killed at the end of the procedure or, if appropriate, during the procedure.

VII. The living conditions of animals should be appropriate for their species and contribute to their health and comfort. Normally, the housing, feeding, and care of all animals used for biomedical purposes must be directed by a veterinarian or other scientist trained and experienced in the proper care, handling, and use of the species being maintained or studied. In any case, veterinary care shall be provided as indicated.

VIII. Investigators and other personnel shall be appropriately qualified and experienced for conducting procedures on living animals. Adequate arrangements shall be made for their in-service training, including the proper and humane care and use of laboratory animals.

IX. Where exceptions are required in relation to the provisions of these Principles, the decisions should not rest with the investigators directly concerned but should be made, with due regard to

Principle II, by an appropriate review group such as an institutional animal care and use committee. Such exceptions should not be made solely for the purposes of teaching or demonstration.



# U.S. Department of Agriculture Animal Welfare Regulations

The full-text of this document may be found at <http://www.aphis.usda.gov/reac/awainfo.html>

## TITLE 9 CODE OF FEDERAL REGULATIONS

### CHAPTER 1

9 CFR Ch. I (1994 Edition)  
Animal and Plant Health Inspection Service, USDA

#### SUBCHAPTER A - ANIMAL WELFARE

#### PART 1 - DEFINITION OF TERMS

Authority: 7 U.S.C. 2131-2157; 7 CFR 2.17, 2.51, and 371.2(g).

##### § 1.1 Definitions.

For the purposes of this subchapter, unless the context otherwise requires, the following terms shall have the meanings assigned to them in this section. The singular form shall also signify the plural and the masculine form shall also signify the feminine. Words undefined in the following paragraphs shall have the meaning attributed to them in general usage as reflected by definitions in a standard dictionary.

*Act* means the Act of August 24, 1966 (Pub. L. 89-544), (commonly known as the Laboratory Animal Welfare Act), as amended by the Act of December 24, 1970 (Pub. L. 91-579), (the Animal Welfare Act of 1970), the Act of April 22, 1976 (Pub. L. 94-279), (the Animal Welfare Act of 1976), and the Act of December 23, 1985 (Pub. L. 99-198), (the Food Security Act of 1985), and as it may be subsequently amended.

*Activity* means, for purposes of part 2, subpart C of this subchapter, those elements of research, testing, or teaching procedures that involve the care and use of animals.

*Administrative unit* means the organizational or management unit at the departmental level of a research facility.

*Administrator* means the Administrator of the Animal and Plant Health Inspection Service, U.S. Department of Agriculture, or any other official of the Animal and Plant Health Inspection Service to whom authority has been delegated to act in his stead.

*Ambient* temperature means the air temperature surrounding the animal.

*Animal* means any live or dead dog, cat, nonhuman primate, guinea pig, hamster, rabbit, or any other warm-blooded animal, which is being used, or is intended for use for research, testing, experimentation, or exhibition purposes, or as a pet. This term excludes: Birds, rats of the genus *Rattus* and mice of the genus *Mus* bred for use in research, and horses not used for research purposes and other farm animals, such as, but not limited to livestock or poultry, used or intended for use as food or fiber, or livestock or poultry used or intended for use for improving animal nutrition,

breeding, management, or production efficiency, or for improving the quality of food or fiber. With respect to a dog, the term means all dogs, including those used for hunting, security, or breeding purposes.

*Animal act* means any performance of animals where such animals are trained to perform some behavior or action or are part of a show, performance, or exhibition.

*APHIS* means the Animal and Plant Health Inspection Service, United States Department of Agriculture.

*APHIS official* means any person employed by the Department who is authorized to perform a function under the Act and the regulations in 9 CFR parts 1, 2, and 3.

*APHIS, REAC Sector Supervisor* means a veterinarian or his designee, employed by APHIS, who is assigned by the Administrator to supervise and perform the official work of APHIS in a given State or States. As used in part 2 of this subchapter, the APHIS, REAC Sector Supervisor shall be deemed to be the person in charge of the official work of APHIS in the State in which the dealer, exhibitor, research facility, intermediate handler, carrier, or operator of an auction sale has his principal place of business.

*Attending veterinarian* means a person who has graduated from a veterinary school accredited by the American Veterinary Medical Association's Council on Education, or has a certificate issued by the American Veterinary Medical Association's Education Commission for Foreign Veterinary Graduates, or has received equivalent formal education as determined by the Administrator; has received training and/or experience in the care and management of the species being attended; and who has direct or delegated authority for activities involving animals at a facility subject to the jurisdiction of the Secretary.

*Business hours* means a reasonable number of hours between 7 a.m. and 7 p.m., Monday through Friday, except for legal Federal holidays, each week of the year, during which inspections by APHIS may be made.

*Business year* means the 12-month period during which business is conducted, and may be either on a calendar or fiscal-year basis.

*Carrier* means the operator of any airline, railroad, motor carrier, shipping line, or other enterprise which is engaged in the business of transporting any animals for hire.

*Cat* means any live or dead cat (*Felis catus*) or any cat-hybrid cross.

*Class "A" licensee* (breeder) means a person subject to the licensing requirements under part 2 and meeting the definition of a "dealer" (§ 1.1), and whose business involving animals consists only of animals that are bred and raised on the premises in a closed or stable colony and those animals acquired for the sole purpose of maintaining or enhancing the breeding colony.

*Class "B" licensee* means a person subject to the licensing requirements under part 2 and meeting the definition of a "dealer" (§ 1.1), and whose business includes the purchase and/or resale of any animal. This term includes brokers, and operators of an auction sale, as such individuals negotiate or arrange for the purchase, sale, or transport of animals in commerce. Such individuals do not usually take actual physical possession or control of the animals, and do not usually hold animals in any facilities. A class "B" licensee may also exhibit animals as a minor part of the business.

*Class "C" licensee* (exhibitor) means a person subject to the licensing requirements under part 2 and meeting the definition of an "exhibitor" (§ 1.1), and whose business involves the showing or displaying of animals to the public. A class "C" licensee may buy and sell animals as a minor part of the business in order to maintain or add to his animal collection.

*Commerce* means trade, traffic, transportation, or other commerce:

(1) Between a place in a State and any place outside of such State, including any foreign country, or between points within the same State but through any place outside thereof, or within any

territory, possession, or the District of Columbia; or

(2) Which affects the commerce described in this part.

*Committee* means the Institutional Animal Care and Use Committee (IACUC) established under section 13(b) of the Act. It shall consist of at least three (3) members, one of whom is the attending veterinarian of the research facility and one of whom is not affiliated in any way with the facility other than as a member of the committee, however, if the research facility has more than one Doctor of Veterinary Medicine (DVM), another DVM with delegated program responsibility may serve. The research facility shall establish the Committee for the purpose of evaluating the care, treatment, housing, and use of animals, and for certifying compliance with the Act by the research facility.

*Dealer* means any person who, in commerce, for compensation or profit, delivers for transportation, or transports, except as a carrier, buys, or sells, or negotiates the purchase or sale of: Any dog or other animal whether alive or dead (including unborn animals, organs, limbs, blood, serum, or other parts) for research, teaching, testing, experimentation, exhibition, or for use as a pet; or any dog for hunting, security, or breeding purposes. This term does not include: A retail pet store, as defined in this section, unless such store sells any animals to a research facility, an exhibitor, or a dealer (wholesale); or any person who does not sell, or negotiate the purchase or sale of any wild or exotic animal, dog, or cat and who derives no more than \$500 gross income from the sale of animals other than wild or exotic animals, dogs, or cats, during any calendar year.

*Department* means the U.S. Department of Agriculture.

*Deputy Administrator* means the Deputy Administrator for Regulatory Enforcement and Animal Care (REAC) or any other official of REAC to whom authority has been delegated to act in his stead.

*Dog* means any live or dead dog (*Canis familiaris*) or any dog-hybrid cross.

*Dwarf hamster* means any species of hamster such as the Chinese and Armenian species whose adult body size is substantially less than that attained by the Syrian or Golden species of hamsters.

*Endangered species* means those species defined in the Endangered Species Act (16 U.S.C. 1531 *et seq.*) and as it may be subsequently amended.

*Euthanasia* means the humane destruction of an animal accomplished by a method that produces rapid unconsciousness and subsequent death without evidence of pain or distress, or a method that utilizes anesthesia produced by an agent that causes painless loss of consciousness and subsequent death.

*Exhibitor* means any person (public or private) exhibiting any animals, which were purchased in commerce or the intended distribution of which affects commerce, or will affect commerce, to the public for compensation, as determined by the Secretary. This term includes carnivals, circuses, animal acts, zoos, and educational exhibits, exhibiting such animals whether operated for profit or not. This term excludes retail pet stores, horse and dog races, organizations sponsoring and all persons participating in State and county fairs, livestock shows, rodeos, field trials, coursing events, purebred dog and cat shows and any other fairs or exhibitions intended to advance agricultural arts and sciences as may be determined by the Secretary.

*Exotic animal* means any animal not identified in the definition of "animal" provided in this part that is native to a foreign country or of foreign origin or character, is not native to the United States, or was introduced from abroad. This term specifically includes animals such as, but not limited to, lions, tigers, leopards, elephants, camels, antelope, anteaters, kangaroos, and water buffalo, and species of foreign domestic cattle, such as Ankole, Gayal, and Yak.

*Farm animal* means any domestic species of cattle, sheep, swine, goats, llamas, or horses,



which are normally and have historically, been kept and raised on farms in the United States, and used or intended for use as food or fiber, or for improving animal nutrition, breeding, management, or production efficiency, or for improving the quality of food or fiber. This term also includes animals such as rabbits, mink, and chinchilla, when they are used solely for purposes of meat or fur, and animals such as horses and llamas when used solely as work and pack animals.

*Federal agency* means an Executive agency as such term is defined in section 105 of title 5, United States Code, and with respect to any research facility means the agency from which the research facility receives a Federal award for the conduct of research, experimentation, or testing involving the use of animals.

*Federal award* means any mechanism (including a grant, award, loan, contract, or cooperative agreement) under which Federal funds are used to support the conduct of research, experimentation, or testing, involving the use of animals. The permit system established under the authorities of the Endangered Species Act, the Marine Mammal Protection Act, and the Migratory Bird Treaty Act, are not considered to be Federal awards under the Animal Welfare Act.

*Federal research facility* means each department, agency, or instrumentality of the United States which uses live animals for research or experimentation.

*Field study* means any study conducted on free-living wild animals in their natural habitat, which does not involve an invasive procedure, and which does not harm or materially alter the behavior of the animals under study. **[Editors note: USDA is in the process of revising this definition. The final notice should be published sometime in the Fall 1999.]**

*Handling* means petting, feeding, watering, cleaning, manipulating, loading, crating, shifting, transferring, immobilizing, restraining, treating, training, working and moving, or any similar activity with respect to any animal.

*Housing facility* means any land, premises, shed, barn, building, trailer, or other structure or area housing or intended to house animals.

*Hybrid cross* means an animal resulting from the crossbreeding between two different species or types of animals. Crosses between wild animal species, such as lions and tigers, are considered to be wild animals. Crosses between wild animal species and domestic animals, such as dogs and wolves or buffalo and domestic cattle, are considered to be domestic animals.

*Impervious surface* means a surface that does not permit the absorption of fluids. Such surfaces are those that can be thoroughly and repeatedly cleaned and disinfected, will not retain odors, and from which fluids bead up and run off or can be removed without their being absorbed into the surface material.

*Indoor housing facility* means any structure or building with environmental controls housing or intended to house animals and meeting the following three requirements:

- (1) It must be capable of controlling the temperature within the building or structure within the limits set forth for that species of animal, of maintaining humidity levels of 30 to 70 percent and of rapidly eliminating odors from within the building; and
- (2) It must be an enclosure created by the continuous connection of a roof, floor, and walls (a shed or barn set on top of the ground does not have a continuous connection between the walls and the ground unless a foundation and floor are provided); and
- (3) It must have at least one door for entry and exit that can be opened and closed (any windows or openings which provide natural light must be covered with a transparent material such as glass or hard plastic).

*Intermediate handler* means any person, including a department, agency, or instrumentality of the United States or of any State or local government (other than a dealer, research facility, exhibitor, any person excluded from the definition of a dealer, research facility, or exhibitor, an

operator of an auction sale, or a carrier), who is engaged in any business in which he receives custody of animals in connection with their transportation in commerce.

*Inspector* means any person employed by the Department who is authorized to perform a function under the Act and the regulations in 9 CFR parts 1, 2, and 3.

*Institutional official* means the individual at a research facility who is authorized to legally commit on behalf of the research facility that the requirements of 9 CFR parts 1, 2, and 3 will be met.

*Isolation* in regard to marine mammals means the physical separation of animals to prevent contact and a separate, noncommon, water circulation and filtration system for the isolated animals.

*Licensed veterinarian* means a person who has graduated from an accredited school of veterinary medicine or has received equivalent formal education as determined by the Administrator, and who has a valid license to practice veterinary medicine in some State.

*Licensee* means any person licensed according to the provisions of the Act and the regulations in part 2 of this subchapter.

*Major operative procedure* means any surgical intervention that penetrates and exposes a body cavity or any procedure which produces permanent impairment of physical or physiological functions.

*Minimum horizontal dimension (MHD)* means the diameter of a circular pool of water, or in the case of a square, rectangle, oblong, or other shape pool, the diameter of the largest circle that can be inserted within the confines of such a pool of water.

*Mobile or traveling housing facility* means a transporting vehicle such as a truck, trailer, or railway car, used to house animals while traveling for exhibition or public education purposes.

*Nonconditioned animals* means animals which have not been subjected to special care and treatment for sufficient time to stabilize, and where necessary, to improve their health.

*Nonhuman primate* means any nonhuman member of the highest order of mammals including prosimians, monkeys, and apes.

*Operator of an auction sale* means any person who is engaged in operating an auction at which animals are purchased or sold in commerce.

*Outdoor housing facility* means any structure, building, land, or premise, housing or intended to house animals, which does not meet the definition of any other type of housing facility provided in the regulations, and in which temperatures cannot be controlled within set limits.

*Painful procedure* as applied to any animal means any procedure that would reasonably be expected to cause more than slight or momentary pain or distress in a human being to which that procedure was applied, that is, pain in excess of that caused by injections or other minor procedures.

*Paralytic drug* means a drug which causes partial or complete loss of muscle contraction and which has no anesthetic or analgesic properties, so that the animal cannot move, but is completely aware of its surroundings and can feel pain.

*Person* means any individual, partnership, firm, joint stock company, corporation, association, trust, estate, or other legal entity.

*Pet animal* means any animal that has commonly been kept as a pet in family households in the United States, such as dogs, cats, guinea pigs, rabbits, and hamsters. This term excludes exotic animals and wild animals.

*Positive physical contact* means petting, stroking, or other touching, which is beneficial to the well-being of the animal.

*Pound or shelter* means a facility that accepts and/or seizes animals for the purpose of caring for them, placing them through adoption, or carrying out law enforcement, whether or not the facility is operated for profit.



*Primary conveyance* means the main method of transportation used to convey an animal from origin to destination, such as a motor vehicle, plane, ship, or train.

*Primary enclosure* means any structure or device used to restrict an animal or animals to a limited amount of space, such as a room, pen, run, cage, compartment, pool, hutch, or tether. In the case of animals restrained by a tether (e.g., dogs on chains), it includes the shelter and the area within reach of the tether.

*Principal investigator* means an employee of a research facility, or other person associated with a research facility, responsible for a proposal to conduct research and for the design and implementation of research involving animals.

*Quorum* means a majority of the Committee members.

*Random source* means dogs and cats obtained from animal pounds or shelters, auction sales, or from any person who did not breed and raise them on his or her premises.

*Registrant* means any research facility, carrier, intermediate handler, or exhibitor not required to be licensed under section 3 of the Act, registered pursuant to the provisions of the Act and the regulations in part 2 of this subchapter.

*Research facility* means any school (except an elementary or secondary school), institution, organization, or person that uses or intends to use live animals in research, tests, or experiments, and that (1) purchases or transports live animals in commerce, or (2) receives funds under a grant, award, loan, or contract from a department, agency, or instrumentality of the United States for the purpose of carrying out research, tests, or experiments: *Provided*, That the Administrator may exempt, by regulation, any such school, institution, organization, or person that does not use or intend to use live dogs or cats, except those schools, institutions, organizations, or persons, which use substantial numbers (as determined by the Administrator) of live animals the principal function of which schools, institutions, organizations, or persons, is biomedical research or testing, when in the judgment of the Administrator, any such exemption does not vitiate the purpose of the Act.

*Retail pet store* means any outlet where only the following animals are sold or offered for sale, at retail, for use as pets: Dogs, cats, rabbits, guinea pigs, hamsters, gerbils, rats, mice, gophers, chinchilla, domestic ferrets, domestic farm animals, birds, and coldblooded species. Such definition excludes--

(1) Establishments or persons who deal in dogs used for hunting, security, or breeding purposes;

(2) Establishments or persons exhibiting, selling, or offering to exhibit or sell any wild or exotic or other nonpet species of warm-blooded animals (except birds), such as skunks, raccoons, nonhuman primates, squirrels, ocelots, foxes, coyotes, etc.;

(3) Any establishment or person selling warm-blooded animals (except birds, and laboratory rats and mice) for research or exhibition purposes; and

(4) Any establishment wholesaling any animals (except birds, rats and mice).

(5) Any establishment exhibiting pet animals in a room that is separate from or adjacent to the retail pet store, or in an outside area, or anywhere off the retail pet store premises.

*Sanitize* means to make physically clean and to remove and destroy, to the maximum degree that is practical, agents injurious to health.

*Secretary* means the Secretary of Agriculture of the United States or his representative who shall be an employee of the Department.

*Sheltered housing facility* means a housing facility which provides the animals with shelter; protection from the elements; and protection from temperature extremes at all times. A sheltered housing facility may consist of runs or pens totally enclosed in a barn or building, or of connecting inside/outside runs or pens with the inside pens in a totally enclosed building.



*Standards* means the requirements with respect to the humane housing, exhibition, handling, care, treatment, temperature, and transportation of animals by dealers, exhibitors research facilities, carriers, intermediate handlers, and operators of auction sales as set forth in part 3 of this subchapter.

*State* means a State of the United States, the District of Columbia, Commonwealth of Puerto Rico, the Virgin Islands, Guam, American Samoa, or any other territory or possession of the United States.

*Study area* means any building room, area, enclosure, or other containment outside of a core facility or centrally designated or managed area in which animals are housed for more than 12 hours.

*Transporting device* means an interim vehicle or device, other than man, used to transport an animal between the primary conveyance and the terminal facility or in and around the terminal facility of a carrier or intermediate handler.

*Transporting vehicle* means any truck, car, trailer, airplane, ship, or railroad car used for transporting animals.

*Weaned* means that an animal has become accustomed to take solid food and has so done, without nursing, for a period of at least 5 days.

*Wild animal* means any animal which is now or historically has been found in the wild, or in the wild state, within the boundaries of the United States, its territories, or possessions. This term includes, but is not limited to, animals such as: Deer, skunk, opossum, raccoon, mink, armadillo, coyote, squirrel, fox, wolf.

*Wild state* means living in its original, natural condition; not domesticated.

*Zoo* means any park, building, cage, enclosure, or other structure or premise in which a live animal or animals are kept for public exhibition or viewing, regardless of compensation.

[54 FR 36119, Aug. 31, 1989, as amended at 55 FR 12631, Apr. 5, 1990]

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**§ 2.31 Institutional Animal Care and Use Committee (IACUC).**

(a) The Chief Executive Officer of the research facility shall appoint an Institutional Animal Care and Use Committee (IACUC), qualified through the experience and expertise of its members to assess the research facility's animal program, facilities, and procedures. Except as specifically authorized by law or these regulations, nothing in this part shall be deemed to permit the Committee or IACUC to prescribe methods or set standards for the design, performance, or conduct of actual research or experimentation by a research facility.

(b) IACUC Membership. (1) The members of each Committee shall be appointed by the Chief Executive Officer of the research facility;

(2) The Committee shall be composed of a Chairman and at least two additional members;

(3) Of the members of the Committee:

(i) At least one shall be a Doctor of Veterinary Medicine, with training or experience in laboratory animal science and medicine, who has direct or delegated program responsibility for activities involving animals at the research facility;

(ii) At least one shall not be affiliated in any way with the facility other than as a member of the Committee, and shall not be a member of the immediate family of a person who is affiliated with the facility. The Secretary intends that such person will provide representation for general community interests in the proper care and treatment of animals;

(4) If the Committee consists of more than three members, not more than three members shall be from the same administrative unit of the facility.

(c) IACUC Functions. With respect to activities involving animals, the IACUC, as an agent of the research facility, shall:

(1) Review, at least once every six months, the research facility's program for humane care and use of animals, using title 9, chapter I, subchapter A-Animal Welfare, as a basis for evaluation;

(2) Inspect, at least once every six months, all of the research facility's animal facilities, including animal study areas, using title 9, chapter I, subchapter A - Animal Welfare, as a basis for evaluation; Provided, however, That animal areas containing free-living wild animals in their natural habitat need not be included in such inspection;

(3) Prepare reports of its evaluations conducted as required by paragraphs (c) (1) and (2) of this section, and submit the reports to the Institutional Official of the research facility; Provided, however, That the IACUC may determine the best means of conducting evaluations of the research facility's programs and facilities; and Provided, further, That no Committee member wishing to participate in any evaluation conducted under this subpart may be excluded. The IACUC may use subcommittees composed of at least two Committee members and may invite ad hoc consultants to assist in conducting the evaluations, however, the IACUC remains responsible for the evaluations and reports as required by the Act and regulations. The reports shall be reviewed and signed by a majority of the IACUC members and must include any minority views. The reports shall be updated at least once every six months upon completion of the required semiannual evaluations and shall be maintained by the research facility and made available to APHIS and to officials of funding Federal agencies for inspection and copying upon request. The reports must contain a description of the nature and extent of the research facility's adherence to this subchapter, must identify specifically any departures from the provisions of title 9, chapter I, subchapter A-Animal Welfare, and must state the reasons for each departure. The reports must distinguish significant deficiencies from minor deficiencies. A significant deficiency is one which, with reference to Subchapter A, and, in the judgment of the IACUC and the Institutional Official, is or may be a threat to the health or safety of the animals. If program or facility deficiencies are noted, the reports must contain a reasonable and specific plan and schedule with dates for correcting each deficiency. Any failure to adhere to the plan and schedule that results in a significant deficiency remaining uncorrected shall be reported in writing within 15 business days by the IACUC, through the Institutional Official, to APHIS and any Federal agency funding that activity;

(4) Review, and, if warranted, investigate concerns involving the care and use of animals at the research facility resulting from public complaints received and from reports of noncompliance received from laboratory or research facility personnel or employees;

(5) Make recommendations to the Institutional Official regarding any aspect of the research facility's animal program, facilities, or personnel training;

(6) Review and approve, require modifications in (to secure approval), or withhold approval of those components of proposed activities related to the care and use of animals, as specified in paragraph (d) of this section;

(7) Review and approve, require modifications in (to secure approval), or withhold approval of proposed significant changes regarding the care and use of animals in ongoing activities; and

(8) Be authorized to suspend an activity involving animals in accordance with the specifications set forth in paragraph (d)(6) of this section.

(d) IACUC review of activities involving animals. (1) In order to approve proposed activities or proposed significant changes in ongoing activities, the IACUC shall conduct a review of those components of the activities related to the care and use of animals and determine that the proposed activities are in accordance with this subchapter unless acceptable justification for a departure is presented in writing; Provided, however, That field studies as defined in part 1 of this subchapter are

exempt from this requirement. Further, the IACUC shall determine that the proposed activities or significant changes in ongoing activities meet the following requirements:

(i) Procedures involving animals will avoid or minimize discomfort, distress, and pain to the animals;

(ii) The principal investigator has considered alternatives to procedures that may cause more than momentary or slight pain or distress to the animals, and has provided a written narrative description of the methods and sources, e.g., the Animal Welfare Information Center, used to determine that alternatives were not available;

(iii) The principal investigator has provided written assurance that the activities do not unnecessarily duplicate previous experiments;

(iv) Procedures that may cause more than momentary or slight pain or distress to the animals will:

(A) Be performed with appropriate sedatives, analgesics or anesthetics, unless withholding such agents is justified for scientific reasons, in writing, by the principal investigator and will continue for only the necessary period of time;

(B) Involve, in their planning, consultation with the attending veterinarian or his or her designee;

(C) Not include the use of paralytics without anesthesia;

(v) Animals that would otherwise experience severe or chronic pain or distress that cannot be relieved will be painlessly euthanized at the end of the procedure or, if appropriate, during the procedure;

(vi) The animals' living conditions will be appropriate for their species in accordance with part 3 of this subchapter, and contribute to their health and comfort. The housing, feeding, and nonmedical care of the animals will be directed by the attending veterinarian or other scientist trained and experienced in the proper care, handling, and use of the species being maintained or studied;

(vii) Medical care for animals will be available and provided as necessary by a qualified veterinarian;

(viii) Personnel conducting procedures on the species being maintained or studied will be appropriately qualified and trained in those procedures;

(ix) Activities that involve surgery include appropriate provision for pre-operative and post-operative care of the animals in accordance with established veterinary medical and nursing practices. All survival surgery will be performed using aseptic procedures, including surgical gloves, masks, sterile instruments, and aseptic techniques. Major operative procedures on non-rodents will be conducted only in facilities intended for that purpose which shall be operated and maintained under aseptic conditions. Non-major operative procedures and all surgery on rodents do not require a dedicated facility, but must be performed using aseptic procedures. Operative procedures conducted at field sites need not be performed in dedicated facilities, but must be performed using aseptic procedures;

(x) No animal will be used in more than one major operative procedure from which it is allowed to recover, unless:

(A) Justified for scientific reasons by the principal investigator, in writing;

(B) Required as routine veterinary procedure or to protect the health or well-being of the animal as determined by the attending veterinarian; or

(C) In other special circumstances as determined by the Administrator on an individual basis. Written requests and supporting data should be sent to the Administrator, APHIS, USDA, 4700 River Road, Suite 6D02, Riverdale, Maryland 20737-1234;



(xi) Methods of euthanasia used must be in accordance with the definition of the term set forth in 9 CFR part 1, § 1.1 of this subchapter, unless a deviation is justified for scientific reasons, in writing, by the investigator.

(2) Prior to IACUC review, each member of the Committee shall be provided with a list of proposed activities to be reviewed. Written descriptions of all proposed activities that involve the care and use of animals shall be available to all IACUC members, and any member of the IACUC may obtain, upon request, full Committee review of those activities. If full Committee review is not requested, at least one member of the IACUC, designated by the chairman and qualified to conduct the review, shall review those activities, and shall have the authority to approve, require modifications in (to secure approval), or request full Committee review of any of those activities. If full Committee review is requested for a proposed activity, approval of that activity may be granted only after review, at a convened meeting of a quorum of the IACUC, and with the approval vote of a majority of the quorum present. No member may participate in the IACUC review or approval of an activity in which that member has a conflicting interest (e.g., is personally involved in the activity), except to provide information requested by the IACUC, nor may a member who has a conflicting interest contribute to the constitution of a quorum;

(3) The IACUC may invite consultants to assist in the review of complex issues arising out of its review of proposed activities. Consultants may not approve or withhold approval of an activity, and may not vote with the IACUC unless they are also members of the IACUC;

(4) The IACUC shall notify principal investigators and the research facility in writing of its decision to approve or withhold approval of those activities related to the care and use of animals, or of modifications required to secure IACUC approval. If the IACUC decides to withhold approval of an activity, it shall include in its written notification a statement of the reasons for its decision and give the principal investigator an opportunity to respond in person or in writing. The IACUC may reconsider its decision, with documentation in Committee minutes, in light of the information provided by the principal investigator;

(5) The IACUC shall conduct continuing reviews of activities covered by this subchapter at appropriate intervals as determined by the IACUC, but not less than annually;

(6) The IACUC may suspend an activity that it previously approved if it determines that the activity is not being conducted in accordance with the description of that activity provided by the principal investigator and approved by the Committee. The IACUC may suspend an activity only after review of the matter at a convened meeting of a quorum of the IACUC and with the suspension vote of a majority of the quorum present;

(7) If the IACUC suspends an activity involving animals, the Institutional Official, in consultation with the IACUC, shall review the reasons for suspension, take appropriate corrective action, and report that action with a full explanation to APHIS and any Federal agency funding that activity; and

(8) Proposed activities and proposed significant changes in ongoing activities that have been approved by the IACUC may be subject to further appropriate review and approval by officials of the research facility. However, those officials may not approve an activity involving the care and use of animals if it has not been approved by the IACUC.

(e) A proposal to conduct an activity involving animals, or to make a significant change in an ongoing activity involving animals, must contain the following:

(1) Identification of the species and the approximate number of animals to be used;

(2) A rationale for involving animals, and for the appropriateness of the species and numbers of animals to be used;

(3) A complete description of the proposed use of the animals;

(4) A description of procedures designed to assure that discomfort and pain to animals will be limited to that which is unavoidable for the conduct of scientifically valuable research, including provision for the use of analgesic, anesthetic, and tranquilizing drugs where indicated and appropriate to minimize discomfort and pain to animals; and

(5) A description of any euthanasia method to be used.

### **§ 2.32 Personnel qualifications.**

(a) It shall be the responsibility of the research facility to ensure that all scientists, research technicians, animal technicians, and other personnel involved in animal care, treatment, and use are qualified to perform their duties. This responsibility shall be fulfilled in part through the provision of training and instruction to those personnel.

(b) Training and instruction shall be made available, and the qualifications of personnel reviewed, with sufficient frequency to fulfill the research facility's responsibilities under this section and § 2.31.

(c) Training and instruction of personnel must include guidance in at least the following areas:

(1) Humane methods of animal maintenance and experimentation, including:

(i) The basic needs of each species of animal;

(ii) Proper handling and care for the various species of animals used by the facility;

(iii) Proper pre-procedural and post-procedural care of animals; and

(iv) Aseptic surgical methods and procedures;

(2) The concept, availability, and use of research or testing methods that limit the use of animals or minimize animal distress;

(3) Proper use of anesthetics, analgesics, and tranquilizers for any species of animals used by the facility;

(4) Methods whereby deficiencies in animal care and treatment are reported, including deficiencies in animal care and treatment reported by any employee of the facility. No facility employee, Committee member, or laboratory personnel shall be discriminated against or be subject to any reprisal for reporting violations of any regulation or standards under the Act;

(5) Utilization of services (e.g., National Agricultural Library, National Library of Medicine) available to provide information:

(i) On appropriate methods of animal care and use;

(ii) On alternatives to the use of live animals in research;

(iii) That could prevent unintended and unnecessary duplication of research involving animals; and

(iv) Regarding the intent and requirements of the Act.

### **§ 2.33 Attending veterinarian and adequate veterinary care.**

(a) Each research facility shall have an attending veterinarian who shall provide adequate veterinary care to its animals in compliance with this section:

(1) Each research facility shall employ an attending veterinarian under formal arrangements. In the case of a part-time attending veterinarian or consultant arrangements, the formal arrangements shall include a written program of veterinary care and regularly scheduled visits to the research facility;

(2) Each research facility shall assure that the attending veterinarian has appropriate authority

to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use; and

(3) The attending veterinarian shall be a voting member of the IACUC; Provided, however, That a research facility with more than one Doctor of Veterinary Medicine (DVM) may appoint to the IACUC another DVM with delegated program responsibility for activities involving animals at the research facility.

(b) Each research facility shall establish and maintain programs of adequate veterinary care that include:

(1) The availability of appropriate facilities, personnel, equipment, and services to comply with the provisions of this subchapter;

(2) The use of appropriate methods to prevent, control, diagnose, and treat diseases and injuries, and the availability of emergency, weekend, and holiday care;

(3) Daily observation of all animals to assess their health and well-being; Provided, however, That daily observation of animals may be accomplished by someone other than the attending veterinarian; and Provided, further, That a mechanism of direct and frequent communication is required so that timely and accurate information on problems of animal health, behavior, and well-being is conveyed to the attending veterinarian;

(4) Guidance to principal investigators and other personnel involved in the care and use of animals regarding handling, immobilization, anesthesia, analgesia, tranquilization, and euthanasia; and

(5) Adequate pre-procedural and post-procedural care in accordance with current established veterinary medical and nursing procedures.

### **§ 2.35 Recordkeeping requirements.**

(a) The research facility shall maintain the following IACUC records:

(1) Minutes of IACUC meetings, including records of attendance, activities of the Committee, and Committee deliberations;

(2) Records of proposed activities involving animals and proposed significant changes in activities involving animals, and whether IACUC approval was given or withheld; and

(3) Records of semiannual IACUC reports and recommendations (including minority views), prepared in accordance with the requirements of § 2.31(c)(3) of this subpart, and forwarded to the Institutional Official.

(b) Every research facility shall make, keep, and maintain records or forms which fully and correctly disclose the following information concerning each live dog or cat purchased or otherwise acquired, owned, held, or otherwise in their possession or under their control, transported, euthanized, sold, or otherwise disposed of by the research facility. The records shall include any offspring born of any animal while in the research facility's possession or under its control:

(1) The name and address of the person from whom a dog or cat was purchased or otherwise acquired, whether or not the person is required to be licensed or registered under the Act;

(2) The USDA license or registration number of the person if he or she is licensed or registered under the Act;

(3) The vehicle license number and state, and the driver's license number and state of the person, if he or she is not licensed or registered under the Act;

(4) The date of acquisition of each dog or cat;

(5) The official USDA tag number or tattoo assigned to each dog or cat under § 2.38(g) of this subpart;



(6) A description of each dog or cat which shall include:

(i) The species and breed or type of animal;

(ii) The sex;

(iii) The date of birth or approximate age; and

(iv) The color and any distinctive markings;

(7) Any identification number or mark assigned to each dog or cat by the research facility.

(c) In addition to the information required to be kept and maintained by every research facility concerning each live dog or cat under paragraph (a) of this section, every research facility transporting, selling, or otherwise disposing of any live dog or cat to another person, shall make and maintain records or forms which fully and correctly disclose the following information:

(1) The name and address of the person to whom a live dog or cat is transported, sold, or otherwise disposed of;

(2) The date of transportation, sale, euthanasia, or other disposition of the animal; and

(3) The method of transportation, including the name of the initial carrier or intermediate handler, or if a privately owned vehicle is used to transport the dog or cat, the name of the owner of the privately owned vehicle.

(d)(1) The USDA Interstate and International Certificate of Health Examination for Small Animals (VS Form 18-1) and Record of Dogs and Cats on Hand (VS Form 18-5) are forms which may be used by research facilities to keep and maintain the information required by paragraph (b) of this section.

(2) The USDA Interstate and International Certificate of Health Examination for Small Animals (VS Form 18-1) and Record of Disposition of Dogs and Cats (VS Form 18-6) are forms which may be used by research facilities to keep and maintain the information required by paragraph (c) of this section.

(e) One copy of the record containing the information required by paragraphs (b) and (c) of this section shall accompany each shipment of any live dog or cat sold or otherwise disposed of by a research facility. Provided, however, That, except as provided by in section 2.133 of this part, information that indicates the source and date of acquisition of any dog or cat need not appear on the copy of the record accompanying the shipment. One copy of the record containing the information required by paragraphs (b) and (c) of this section shall be retained by the research facility.

(f) All records and reports shall be maintained for at least three years. Records that relate directly to proposed activities and proposed significant changes in ongoing activities reviewed and approved by the IACUC shall be maintained for the duration of the activity and for an additional three years after completion of the activity. All records shall be available for inspection and copying by authorized APHIS or funding Federal agency representatives at reasonable times. APHIS inspectors will maintain the confidentiality of the information and will not remove the materials from the research facilities' premises unless there has been an alleged violation, they are needed to investigate a possible violation, or for other enforcement purposes. Release of any such materials, including reports, summaries, and photographs that contain trade secrets or commercial or financial information that is privileged or confidential will be governed by applicable sections of the Freedom of Information Act. Whenever the Administrator notifies a research facility in writing that specified records shall be retained pending completion of an investigation or proceeding under the Act, the research facility shall hold those records until their disposition is authorized in writing by the Administrator.

## **§ 2.36 Annual report.**

(a) The reporting facility shall be that segment of the research facility, or that department, agency, or instrumentality of the United States, that uses or intends to use live animals in research, tests, experiments, or for teaching. Each reporting facility shall submit an annual report to the APHIS, REAC Sector Supervisor for the State where the facility is located on or before December 1 of each calendar year. The report shall be signed and certified by the CEO or Institutional Official, and shall cover the previous Federal fiscal year.

(b) The annual report shall:

(1) Assure that professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during, and following actual research, teaching, testing, surgery, or experimentation were followed by the research facility;

(2) Assure that each principal investigator has considered alternatives to painful procedures;

(3) Assure that the facility is adhering to the standards and regulations under the Act, and that it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the IACUC. A summary of all such exceptions must be attached to the facility's annual report. In addition to identifying the IACUC-approved exceptions, this summary must include a brief explanation of the exceptions, as well as the species and number of animals affected;

(4) State the location of all facilities where animals were housed or used in actual research, testing, teaching, or experimentation, or held for these purposes;

(5) State the common names and the numbers of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs. Routine procedures (e.g., injections, tattooing, blood sampling) should be reported with this group;

(6) State the common names and the numbers of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used;

(7) State the common names and the numbers of animals upon which teaching, experiments, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. An explanation of the procedures producing pain or distress in these animals and the reasons such drugs were not used shall be attached to the annual report;

(8) State the common names and the numbers of animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes.

## **§ 2.37 Federal research facilities.**

Each Federal research facility shall establish an Institutional Animal Care and Use Committee which shall have the same composition, duties, and responsibilities required of nonfederal research facilities by § 2.31 with the following exceptions:

(a) The Committee shall report deficiencies to the head of the Federal agency conducting the research rather than to APHIS; and

(b) The head of the Federal agency conducting the research shall be responsible for all corrective action to be taken at the facility and for the granting of all exceptions to inspection protocol.

## § 2.38 Miscellaneous.

(a) *Information as to business: furnishing of same by research facilities.* Each research facility shall furnish to any APHIS official any information concerning the business of the research facility which the APHIS official may request in connection with the enforcement of the provisions of the Act, the regulations, and the standards in this subchapter. The information shall be furnished within a reasonable time and as may be specified in the request for information.

(b) *Access and inspection of records and property.*

(1) Each research facility shall, during business hours, allow APHIS officials:

(i) To enter its place of business;

(ii) To examine records required to be kept by the Act and the regulations in this part;

(iii) To make copies of the records;

(iv) To inspect the facilities, property, and animals, as the APHIS officials consider necessary to enforce the provisions of the Act, the regulations, and the standards in this subchapter; and

(v) To document, by the taking of photographs and other means, conditions and areas of noncompliance.

(2) The use of a room, table or other facilities necessary for the proper examination of the records and for inspection of the property or animals shall be extended to APHIS officials by the research facility.

(c) *Publication of names of research facilities subject to the provisions of this part.* APHIS will publish lists of research facilities registered in accordance with the provisions of this subpart in the Federal Register. The lists may be obtained upon request from the APHIS, REAC Sector Supervisor.

(d) *Inspection for missing animals.* Each research facility shall allow, upon request and during business hours, police or officers of other law enforcement agencies with general law enforcement authority (not those agencies whose duties are limited to enforcement of local animal regulations) to enter its place of business to inspect animals and records for the purpose of seeking animals that are missing, under the following conditions:

(1) The police or other law officer shall furnish to the research facility a written description of the missing animal and the name and address of its owner before making a search;

(2) The police or other law officer shall abide by all security measures required by the research facility to prevent the spread of disease, including the use of sterile clothing, footwear, and masks where required, or to prevent the escape of an animal.

(e) *Confiscation and destruction of animals.* (1) If an animal being held by a research facility is not being used to carry out research, testing, or experimentation, and is found by an APHIS official to be suffering as a result of the failure of the research facility to comply with any provision of the regulations or the standards set forth in this subchapter, the APHIS official shall make a reasonable effort to notify the research facility of the condition of the animal(s) and request that the condition be corrected and that adequate care be given to alleviate the animal's suffering or distress, or that the animal(s) be destroyed by euthanasia. In the event that the research facility refuses to comply with this request, the APHIS official may confiscate the animal(s) for care, treatment, or disposal as indicated in paragraph (e)(2) of this section, if, in the opinion of the Administrator, the circumstances indicate the animal's health is in danger.

(2) In the event that the APHIS official is unable to locate or notify the research facility as required in this section, the APHIS official shall contact a local police or other law officer to accompany him or her to the premises and shall provide for adequate care when necessary to alleviate the animal's suffering. If, in the opinion of the Administrator, the condition of the animal(s)



cannot be corrected by this temporary care, the APHIS official shall confiscate the animal(s).

(3) Confiscated animals may be placed, by sale or donation, with other registrants or licensees that comply with the standards and regulations and can provide proper care, or they may be euthanized. The research facility from which the animals were confiscated shall bear all costs incurred in performing the placement or euthanasia activities authorized by this section.

(f) *Handling*. (1) Handling of all animals shall be done as expeditiously and carefully as possible in a manner that does not cause trauma, overheating, excessive cooling, behavioral stress, physical harm, or unnecessary discomfort.

(2)(i) Physical abuse shall not be used to train, work, or otherwise handle animals.

(ii) Deprivation of food or water shall not be used to train, work, or otherwise handle animals; *Provided*, however: That the short-term withholding of food or water from animals, when specified in an IACUC-approved activity that includes a description of monitoring procedures, is allowed by these regulations.

# **Selected USDA Animal Care Policies**

All USDA Animal Care Policies may be found at <http://www.aphis.usda.gov/ac/polman.html>

## **Policy #3 --- Veterinary Care--- April 14, 1997**

### **Expired Medical Materials**

### **Pharmaceutical-Grade Compounds in Research**

### **Surgery**

### **Pre- and Post-Procedural Care**

### **Program of Veterinary Care**

### **Euthanasia**

References: AWA Section 13 and 9 CFR, Part 2, Sections 2.31, 2.32, 2.33, 2.40 and 9 CFR, Part 3, Section 3.110

History: Provides requested guidance. Replaces memoranda dated May 31, 1990, November 29, 1991, April 6, 1992, and September 25, 1992.

Justification: The Animal Welfare Act (AWA) requires that all regulated animals be provided adequate veterinary care.

Policy:

### **Expired Medical Materials**

The use of expired medical materials such as drugs, fluids, or sutures on regulated animals is not considered to be acceptable veterinary practice and does not constitute adequate veterinary care as required by the regulations promulgated under the Animal Welfare Act. All expired medical materials found in a licensed or registered facility are to be brought to the attention of the responsible official. The facility must either dispose of all such materials or segregate them in an appropriately labeled, physically separate location from non-expired medical materials. The Animal & Plant Health Inspection Service (APHIS) has no jurisdiction over facilities using expired medical materials for non-regulated animals or non-regulated activities. For acute terminal procedures, APHIS does not oppose the use of expired medical materials if their use does not adversely affect the animal's well-being or compromise the validity of the scientific study. Proper anesthesia, analgesia, and euthanasia are required for all such procedures. Drugs administered to relieve pain or distress and emergency drugs must not be used beyond their expiration date. Facilities allowing the use of expired medical materials in acute terminal procedures should have a policy covering the use of such materials and/or require investigators to describe in their animal activity proposals the intended use of expired materials. The attending veterinarian and the Institutional Animal Care and Use

Committee (IACUC) are responsible for ensuring that proposed animal activities avoid or minimize discomfort, distress, and pain to the animal. These responsibilities cannot be met unless the veterinarian and the IACUC maintain control over the use of expired medical materials.

### **Pharmaceutical-Grade Compounds in Research**

Investigators are expected to use pharmaceutical-grade medications whenever they are available, even in acute procedures. Non-pharmaceutical-grade chemical compounds should only be used in regulated animals after specific review and approval by the IACUC for reasons such as scientific necessity or non-availability of an acceptable veterinary or human pharmaceutical-grade product. Cost savings alone are not an adequate justification for using non-pharmaceutical-grade compounds in regulated animals.

### **Surgery**

AWA regulations require that survival surgeries be performed using aseptic techniques and that major operative procedures on nonrodents be performed only in dedicated surgical facilities. Nonsurvival surgeries require neither aseptic techniques nor dedicated facilities if the subjects are not anesthetized long enough to show evidence of infection. Research facilities doing surgical demonstrations while traveling must use aseptic techniques and dedicated surgical facilities. Motel meeting rooms and auditoriums do not qualify as dedicated surgical facilities. Nonsurvival surgeries not performed aseptically or in a dedicated facility must at least be performed in a clean area, free of clutter, and using acceptable veterinary sanitation practices analogous to those used in a standard examination/treatment room. Personnel present in the area must observe reasonable cleanliness practices for both themselves and the animals. Eating, drinking, or smoking are not acceptable in surgery areas, and locations used for food handling purposes do not qualify as acceptable areas for performing surgeries.

### **Pre- and Post-Procedural Care**

All animal activity proposals involving surgery must provide specific details of pre- through post-procedural care and relief of pain and distress. The specific details must be approved by the attending veterinarian or his/her designee. However, the attending veterinarian retains the authority to change post-operative care as necessary to ensure the comfort of the animal. The withholding of pain and/or distress relieving care must be scientifically justified in writing and approved by the IACUC. The appropriate use of drugs to relieve pain and/or distress must be specified in the animal activity proposal to avoid possible delays due to investigator concerns that a treatment regimen may interfere with the study. Furthermore, the specified drugs for relief of pain and/or distress must be readily available for use as described in the proposal. While an animal is under post-surgical care, the ownership of the animal is not to change. If the animal is taken to an off-site location, such as a farm, for post-operative care, that location should be identified as a site of the research facility. An animal is not to be taken to an off-site location before it fully recovers from anesthesia unless justified in the animal activity proposal. Appropriate post-operative records must be maintained in accordance with professionally accepted veterinary procedures regardless of the location of the animal.



## **Program of Veterinary Care**

Facilities which do not have a full-time attending veterinarian must have a written Program of Veterinary Care (PVC). This Program must consist of a properly completed APHIS Form 7002 or an equivalent format providing all of the information required by the APHIS form. The attending veterinarian must visit the facility on a regular basis, i.e., often enough to provide adequate oversight of the facility's care and use of animals but no less than annually. The PVC must be reviewed annually and updated whenever necessary (e.g., as a new species of animal or a new attending veterinarian is obtained, or the preventive medical program changes). It must be initialed and dated by both the attending veterinarian and the facility representative whenever it is changed or reviewed without change. The preventive medical program described in the PVC is expected to be in accordance with common good veterinary practices (e.g., appropriate vaccinations, diagnostic testing). It should include zoonotic disease prevention measures and, if necessary, special dietary prescriptions.

## **Euthanasia**

The method of euthanasia must be consistent with the current Report of the AVMA Panel on Euthanasia. Gunshot is not an acceptable method of routine euthanasia for any animal. Gunshot as a routine method of euthanasia not only endangers surrounding animals, buildings, and personnel, but it is likely to cause distress to other animals. It should only be used in situations where other forms of acceptable euthanasia cannot be used (such as emergency or field conditions where the animal cannot be appropriately restrained) or in cases where gunshot will reduce danger to other animals or humans. Only personnel skilled in the use of firearms, using appropriate firearms, and familiar with the "kill point" of an animal should perform the euthanasia. If the firearm is not aimed so that the projectile enters the brain and causes rapid unconsciousness and subsequent death without evidence of pain or distress, this method does not meet the definition of euthanasia. (All State and local laws relevant to gunshot must also be met.)

## **Policy #9 --- Barrier Facility SPF Colony Inspection --- April 14, 1997**

References: AWA Section 16 (a) and 9 CFR, Part 2, Sections 2.38(b), 2.1

History: Provides requested guidance. Replaces letter dated July 5, 1991.

Justification: The Animal & Plant Health Inspection Service (APHIS) must have access to inspect all covered animals at a regulated facility to ensure compliance with the Animal Welfare Act (AWA).

Policy:

Animals housed in barrier facilities are required to be maintained in accordance with the AWA's regulations and standards.

In some cases, APHIS inspections of bonafide barrier facilities may be performed by analysis of

environmental records, visual inspection through an adequate viewing window, and random selection of animals to be visually inspected. Various non-entry methods, such as video viewing from outside the barrier room, may substitute for an inadequate viewing window.

If the APHIS inspector determines it is necessary to enter a barrier room to adequately complete an inspection or to resolve a suspected problem, the inspector may, by following entry procedures normally used by facility personnel, enter and complete the inspection. The inspector cannot be expected to comply with procedures not used by facility employees. The facility must supply a copy of their barrier entry procedures upon request. The facility will need to provide the inspector with protective clothing and items needed to complete the inspection (pens, paper, tape measure, flashlight, etc.).

Prior to an inspection of a barrier facility, the facility may ask the inspector (as part of the standard entry procedure) to verify that he/she has not been in contact with, or exposed to, certain animals for a specified time period.

Such verification is acceptable. Generally, barrier facilities require a period of no animal or specific species contact for 72 hours.

The APHIS inspector will not sign any statement in which he or she accepts responsibility for the health of the animals in that barrier facility.

## **Policy #11 --- Painful/Distressful Procedures --- April 14, 1997**

References: AWA Sections 13(a)(3), 13(a)(7), 13(e)(2, 3) and 9 CFR, Part 2, Sections 2.31(d)(1)(i,ii,iii,iv), 2.31(e)(4), 2.33(b)(4) and 9 CFR, Part 3, Section 3.6(b)(5,6,7)

History: Replaces letters dated May 8, 1992, November 7, 1991, November 9, 1990, and March 1, 1990.

Justification: Provides requested guidance. Procedures involving animals will avoid or minimize discomfort, distress and/or pain.

Policy:

A painful procedure is defined as any procedure that would reasonably be expected to cause more than slight or momentary pain and/or distress in a human being to which that procedure is applied. The Institutional Animal Care and Use Committee (IACUC) is responsible for ensuring that investigators have appropriately considered alternatives to any procedures that may cause more than slight or momentary pain or distress. A written narrative description of the methods and sources used to search for alternatives must be provided. Where specific testing procedures are required by Federal law, the CFR references or other legal guidelines requiring them should be noted.

Examples of procedures that can be expected to cause more than momentary or slight pain include,

but are not limited to, the following:

- ★ Terminal Surgery is considered a painful procedure which is alleviated by anesthesia.
- ★ Freund's Complete Adjuvant used for antibody production may cause results ranging from momentary or slight pain to severe pain depending on the product, procedure, and species.
- ★ Ocular and Skin Irritancy Testing. The dosing procedure itself is generally not painful but the reaction caused by the product being tested may cause pain.

Examples of procedures that may cause more than momentary or slight distress include, but are not limited to, the following:

- ★ Food or water deprivation beyond that necessary for normal presurgical preparation.
- ★ Noxious electrical shock that is not immediately escapable.
- ★ Paralysis or immobility in a conscious animal.

Many procedures, including any of those in the lists above, may cause both pain and distress. An example of a procedure that can be expected to cause more than momentary or slight pain as well as distress would be a study involving extensive irradiation.

Animals exhibiting signs of pain, discomfort, or distress such as decreased appetite/activity level, adverse reactions to touching inoculated areas, open sores/necrotic skin lesions, abscesses, lameness, conjunctivitis, corneal edema, and photophobia are expected to receive appropriate relief unless written scientific justification is provided in the animal activity proposal and approved by the IACUC.

Research facilities must have a mechanism in place for ensuring that animals are reported in the appropriate pain category on the annual report (APHIS Form 7023). Individual animals that do not experience pain/distress from testing procedures should be reported in column C. Individual animals experiencing pain/distress which is alleviated with anesthetics, analgesics, sedatives and/or tranquilizers should be reported in column D. This category includes terminal surgery under anesthesia. Individual animals in which needed anesthetics, analgesics, sedatives, and/or tranquilizers are withheld should be reported in column E. For all column E animals, a written justification, approved by the IACUC, must be provided, including CFR references or other guidelines if appropriate.

## **Policy #12 --- Written Narrative for Alternatives to Painful Procedures --- April 14, 1997**

References: AWA Section 13(a)(3)(B) and 9 CFR, Part 2, Section 2.31 (d)(1)(ii)

History: Provides requested guidance.

Justification: The Principal Investigator must provide a written narrative of the sources consulted to determine whether or not alternatives exist to procedures which may cause pain or distress.



## Policy:

Consideration of alternatives to each procedure which may cause pain or distress must state sources consulted, such as Biological Abstracts, Index Medicus, Medline, the Current Research Information Service (CRIS), and the Animal Welfare Information Center (AWIC).

The minimal written narrative should include: the databases searched or other sources consulted, the date of the search and the years covered by the search, and the key words and/or search strategy used by the Principal Investigator when considering alternatives or descriptions of other methods and sources used to determine that no alternatives were available to the painful or distressful procedure. The narrative should be such that the IACUC can readily assess whether the search topics were appropriate and whether the search was sufficiently thorough.

Reduction, replacement, and refinement (the three R's) must be addressed, not just animal replacement.

## **Policy #14 --- Major Survival Surgery Single vs. Multiple Procedures --- April 14, 1997**

References: AWA Section 13(a)(3)(D,E) and 9 CFR, Part 2, Section 2.31 (d)(1)(x)

History: Provides requested guidance. Replaces letters dated April 21, 1992 and June 5, 1990.

Justification: No animal is to be used in more than one major survival operative procedure except in cases of scientific necessity or veterinary care.

## Policy:

No animal assigned to a proposal is to be used in more than one major survival operative procedure unless the multiple procedures are included within one proposal, justified for scientific reasons by the Principal Investigator, and preapproved by the Institutional Animal Care and Use Committee (IACUC). However, an animal that has an emergency major operative procedure as part of proper veterinary care may still be used in a proposal that requires a major survival operative procedure.

A major survival operative procedure must not be performed a second time on an animal in a separate proposal. In order to comply with the intent of the Animal Welfare Act (AWA), animals surviving a major operative procedure must be identified (written documentation) to prevent their use in a second major survival operative procedure.

The AWA and its regulations allow an exemption to limiting animals from being used in only one proposal with a major survival operative procedure. The Institutional Official of the research facility should make the exemption request to the appropriate Animal Care Regional Director, who forwards it to the Animal Care Assistant Deputy Administrator for review and recommendation to the Deputy Administrator. The request for exemption should include the following information:

- a. An outline of the research proposals for which the procedure is requested
- b. The species and the approximate number of animals involved in the exemption request
- c. The time frame for the proposed exempt procedure
- d. The number of major operative procedures to be performed on a given animal, the frequency of such procedures, and the period of time between each major operative procedure
- e. Measures to be taken to ensure that pain/distress are minimized
- f. A complete justification for the exemption in which cost is not normally a major criterion
- g. An assurance that all other stipulated requirements of the AWA and regulations will be met in consideration of this exemption
- h. An assurance that the facility's IACUC has approved the exemption.

The Animal & Plant Health Inspection Service (APHIS) may respond to the formal request by approving the request as written, granting a portion of the request, imposing additional limitations, or denying the request. An annual IACUC evaluation of the exemption is required, which consists of an IACUC assessment of the animals and the effectiveness and soundness of the methods and procedures used. This information is to be included in the report of the IACUC functions. Considerations for the renewal or continuation of the exemption will be based on the IACUC's recommendations following their review. The exemption must be included in the Annual Report (APHIS Form 7023).

## **Policy #15 --- IACUC Membership --- April 14, 1997**

References: AWA Section 13(b)(1) and 9 CFR, Part 2, Section 2.31(b)(2,3)

History: Provides requested guidance. Replaces letters dated June 6, 1994 and October 23, 1992.

Justification: To provide clarification of specified individual roles in the Animal Care and Use Program at research facilities.

Policy:

For Animal Welfare Act (AWA) enforcement purposes, the nonaffiliated member of the Institutional Animal Care and Use Committee (IACUC) is to "provide representation for general community interests." The outside nonaffiliated member cannot be a laboratory animal user at any research facility. Compensation of the nonaffiliated member is permissible only when it does not jeopardize the member's status as a nonaffiliated member. Compensation varies but is normally limited to payment for travel and related expenses, such as parking and meals, to modest monetary payments for participation. The dollar amount of compensation, if any, should not be so substantial as to be considered an important source of income or to influence voting on the IACUC.



The regulations provide for four specific roles within the Animal Care and Use Program:

1. Institutional Official
2. IACUC Chairperson
3. Attending Veterinarian
4. Nonaffiliated Member

These positions are meant to provide a system of checks and balances which is not normally achieved if any one person fills more than one of these roles. While the regulations do not specifically prohibit one person from filling more than one role, the Animal and Plant Health Inspection Service (APHIS) strongly discourages such assignments because of the potential for conflicts of interest and/or undue influence by one person over the facility's program. However, a veterinarian who is not the attending veterinarian may assume any one of the other program positions.

No IACUC member can review his/her own proposal.

## **Policy #26 -- Regulation of Agricultural Animals -- November 17, 1998**

References: AWA Section 13  
9 CFR, Part 3, Subpart F

History: Clarifies existing internal policy

Justification: The Animal Welfare Act (AWA) regulations cover farm animals that are used in activities that are regulated by the AWA.

Policy:

Farm animals, such as domestic cattle, horses, sheep, swine, and goats that are used for traditional, production agricultural purposes are exempt from coverage by the AWA. Traditional production agricultural purposes includes use as food and fiber, for improvement of animal nutrition, breeding, management, or production efficiency, or for improvement of the quality of food or fiber.

Farm animals that are used to manufacture and test veterinary biological products intended for use in the diagnosis, treatment, or prevention of diseases in agricultural animals are, therefore, exempt from U.S. Department of Agriculture's (USDA) regulatory authority under the AWA. USDA considers this use to be agricultural research, thus, not a regulated activity.

Farm animals that are used to test and produce biologicals for nonagricultural or nonproduction animals are covered by Part 3, Subpart F of the regulations. We consider this to be nonagricultural research and testing that is covered by the AWA and the regulations. As such, when farm animals are used to test or manufacture vaccines, bacterins, toxoids, and other related veterinary biologicals that will be used exclusively in nonproduction animals such as dogs and cats and other pet animals, or in

both nonproduction, as well as, farm animals, they are regulated and monitored for compliance with the regulations. An example of the latter may include rabies vaccine or other product that has a multi-species label recommendation.

Farm animals that are used as models for human subjects in order to test or manufacture biologicals that will ultimately be used in humans are also regulated. USDA considers this to be biomedical research which is a regulated activity.



# Public Health Service Policy on Humane Care and Use of Laboratory Animals

Revised September, 1986  
Reprinted March, 1996

The full-text of this policy may be found at <http://www.nih.gov:80/grants/oprr/phspol.htm>

## 3. Institutional Animal Care and Use Committee (IACUC)

- a. The Chief Executive Officer shall appoint an Institutional Animal Care and Use Committee (IACUC), qualified through the experience and expertise of its members to oversee the institution's animal program, facilities, and procedures.
- b. The Assurance must include the names, position titles, and credentials of the IACUC chairperson and the members. The committee shall consist of not less than five members, and shall include at least:
  - (1) one Doctor of Veterinary Medicine, with training or experience in laboratory animal science and medicine, who has direct or delegated program authority and responsibility for activities involving animals at the institution (see IV.A.1.c.);
  - (2) one practicing scientist experienced in research involving animals;
  - (3) one member whose primary concerns are in a nonscientific area (for example, ethicist, lawyer, member of the clergy); and
  - (4) one individual who is not affiliated with the institution in any way other than as a member of the IACUC, and is not a member of the immediate family of a person who is affiliated with the institution.
- c. An individual who meets the requirements of more than one of the categories detailed in IV.A.3.b.(1)-(4) of this policy may fulfill more than one requirement. However, no committee may consist of less than five members.

## B. Functions of the Institutional Animal Care and Use Committee

As an agent of the institution, the IACUC shall with respect to PHS - conducted or supported activities:

1. review at least once every six months the institution's program for humane care and use of animals, using the Guide as a basis for evaluation;
2. inspect at least once every six months all of the institution's animal facilities (including satellite facilities) using the Guide as a basis for evaluation;



3.prepare reports of the IACUC evaluations conducted as required by IV.B.1. and 2. of this Policy, and submit the reports to the Institutional Official. (NOTE: the reports shall be updated at least once every six months upon completion of the required semiannual evaluations and shall be maintained by the institution and made available to OPRR upon request. The reports must contain a description of the nature and extent of the institution's adherence to the Guide and this Policy and must identify specifically any departures from the provisions of the Guide and this Policy, and must state the reasons for each departure. The reports must distinguish significant deficiencies from minor deficiencies. A significant deficiency is one which, consistent with this Policy, and, in the judgment of the IACUC and the Institutional Official, is or may be a threat to the health or safety of the animals. If program or facility deficiencies are noted, the reports must contain a reasonable and specific plan and schedule for correcting each deficiency. If some or all of the institution's facilities are accredited by AAALAC or another accrediting body recognized by PHS, the report should identify those facilities as such.);

4.review concerns involving the care and use of animals at the institution;

5.make recommendations to the Institutional Official regarding any aspect of the institution's animal program, facilities, or personnel training;

6.review and approve, require modifications in (to secure approval) or withhold approval of those components of PHS-conducted or supported activities related to the care and use of animals as specified in IV.C. of this Policy;

7.review and approve, require modifications in (to secure approval), or withhold approval of proposed significant changes regarding the use of animals in ongoing activities; and

8.be authorized to suspend an activity involving animals in accordance with the specifications set forth in IV.C.6 of this Policy.

### **C. Review of PHS-Conducted or Supported Research Projects**

1.In order to approve proposed research projects or proposed significant changes in ongoing research projects, the IACUC shall conduct a review of those components related to the care and use of animals and determine that the proposed research projects are in accordance with this Policy. In making this determination, the IACUC shall confirm that the research project will be conducted in accordance with the Animal Welfare Act insofar as it applies to the research project, and that the research project is consistent with the Guide unless acceptable justification for a departure is presented. Further, the IACUC shall determine that the research project conforms with the institution's Assurance and meets the following requirements:

a. Procedures with animals will avoid or minimize discomfort, distress, and pain to the animals, consistent with sound research design.

b. Procedures that may cause more than momentary or slight pain or distress to the animals will be performed with appropriate sedation, analgesia, or anesthesia, unless the procedure is justified for scientific reasons in writing by the investigator.

- c. Animals that would otherwise experience severe or chronic pain or distress that cannot be relieved will be painlessly killed at the end of the procedure or, if appropriate, during the procedure.
- d. The living conditions of animals will be appropriate for their species and contribute to their health and comfort. The housing, feeding, and nonmedical care of the animals will be directed by a veterinarian or other scientist trained and experienced in the proper care, handling, and use of the species being maintained or studied.
- e. Medical care for animals will be available and provided as necessary by a qualified veterinarian.
- f. Personnel conducting procedures on the species being maintained or studied will be appropriately qualified and trained in those procedures.
- g. Methods of euthanasia used will be consistent with the recommendations of the American Veterinary Medical Association (AVMA) Panel on Euthanasia, unless a deviation is justified for scientific reasons in writing by the investigator.

2. Prior to the review, each IACUC member shall be provided with a list of proposed research projects to be reviewed. Written descriptions of research projects that involve the care and use of animals shall be available to all IACUC members, and any member of the IACUC may obtain, upon request, full committee review of those research projects. If full committee review is not requested, at least one member of the IACUC, designated by the chairperson and qualified to conduct the review, shall review those research projects and have the authority to approve, require modifications in (to secure approval) or request full committee review of those research projects. If full committee review is requested, approval of those research projects may be granted only after review at a convened meeting of a quorum of the IACUC and with the approval vote of a majority of the quorum present. No member may participate in the IACUC review or approval of a research project in which the member has a conflicting interest (e.g., is personally involved in the project) except to provide information requested by the IACUC; nor may a member who has a conflicting interest contribute to the constitution of a quorum.

3. The IACUC may invite consultants to assist in the review of complex issues. Consultants may not approve or withhold approval of an activity or vote with the IACUC unless they are also members of the IACUC.

4. The IACUC shall notify investigators and the institution in writing of its decision to approve or withhold approval of those activities related to the care and use of animals, or of modifications required to secure IACUC approval. If the IACUC decides to withhold approval of an activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing.

5. The IACUC shall conduct continuing review of each previously approved, ongoing activity covered by this Policy at appropriate intervals as determined by the IACUC, including a complete review in accordance with IV.C.1.-4. at least once every three years.

6.The IACUC may suspend an activity that it previously approved if it determines that the activity is not being conducted in accordance with applicable provisions of the Animal Welfare Act, the Guide, the institution's Assurance, or IV.C.1.a.-g. of this Policy. The IACUC may suspend an activity only after review of the matter at a convened meeting of a quorum of the IACUC and with the suspension vote of a majority of the quorum present.

7.If the IACUC suspends an activity involving animals, the Institutional Official in consultation with the IACUC shall review the reasons for suspension, take appropriate corrective action, and report that action with a full explanation to OPRR.

8.Applications and proposals that have been approved by the IACUC may be subject to further appropriate review and approval by officials of the institution. However, those officials may not approve an activity involving the care and use of animals if it has not been approved by the IACUC.

#### **D. Information Required in Applications-Proposals for Awards Submitted to PHS**

##### ***1. All Institutions***

Applications and proposals (competing and non-competing) for awards submitted to PHS that involve the care and use of animals shall contain the following information:

- a. identification of the species and approximate number of animals to be used;
- b. rationale for involving animals, and for the appropriateness of the species and numbers to be used;
- c. a complete description of the proposed use of the animals;
- d. a description of procedures designed to assure that discomfort and injury to animals will be limited to that which is unavoidable in the conduct of scientifically valuable research, and that analgesic, anesthetic, and tranquilizing drugs will be used where indicated and appropriate to minimize discomfort and pain to animals; and
- e. a description of any euthanasia method to be used.

Non-competing applications and contract proposals for other than full and open competitions need not repeat the information required by IV.D.1.a.-e. if the information was complete in the last competing application or proposal and there are no significant changes to that information. However, the application or proposal must contain a statement to that effect. If there are significant changes in the information, then the application or proposal must specifically identify them and state the reasons for the changes.

##### ***2. Institutions That Have an Approved Assurance***

Applications or proposals (competing and non-competing) covered by this Policy from institutions which have an approved Assurance on file with OPRR shall include verification of approval (including the date of the most recent approval) by the IACUC of those components related to the care and use of animals. For competing applications or proposals only, such verification may be filed at a time not to exceed 60 days after the receipt deadline date. If verification of IACUC



approval is submitted subsequent to the submission of the application or proposal, the verification shall state the modifications, if any, required by the IACUC. The verification shall be signed by an individual authorized by the institution, but need not be signed by the Institutional Official.

### ***3. Institutions That Do Not Have an Approved Assurance***

For applications and proposals covered by this Policy from institutions that do not have an approved Assurance on file with OPRR, the signature of the official signing for the applicant organization shall constitute a declaration that the institution will submit an Assurance when requested by OPRR. Upon such request, the institution shall prepare the Assurance as instructed by OPRR and in accordance with IV.A. of this Policy. The authorized IACUC shall review those components of the application or proposal as required by IV.C. of this Policy. Upon IACUC approval of those components of the application or proposal the institution shall submit the Assurance to OPRR.

## **E. Recordkeeping Requirements**

1. The awardee institution shall maintain:

- a. a copy of the Assurance which has been approved by the PHS;
- b. minutes of IACUC meetings, including records of attendance, activities of the committee, and committee deliberations;
- c. records of applications, proposals, and proposed significant changes in the care and use of animals and whether IACUC approval was given or withheld;
- d. records of semiannual IACUC reports and recommendations (including minority views) as forwarded to the Institutional Official; and
- e. records of accrediting body determinations.

2. All records shall be maintained for at least three years; records that relate directly to applications, proposals, and proposed significant changes in ongoing activities reviewed and approved by the IACUC shall be maintained for the duration of the activity and for an additional three years after completion of the activity. All records shall be accessible for inspection and copying by authorized OPRR or other PHS representatives at reasonable times and in a reasonable manner.

## **F. Reporting Requirements**

1. At least once every 12 months, the IACUC, through the Institutional Official, shall report in writing to OPRR:

- a. any change in the institution's program or facilities which would place the institution in a different category than specified in its Assurance (see IV.A.2. of this Policy);
- b. any change in the description of the institution's program for animal care and use as required by IV.A.1.a.-i. of this Policy;



c. any changes in the IACUC membership; and

d. notice of the dates that the IACUC conducted its semiannual evaluations of the institution's program and facilities and submitted the evaluations to the Institutional Official.

2. At least once every 12 months, the IACUC, at an institution which has no changes to report as specified in IV.F.1.a.-c. of this Policy, shall submit a letter, through the Institutional Official, to OPRR stating that there are no changes and informing OPRR of the dates of the required IACUC evaluations and submissions to the Institutional Official.

3. The IACUC, through the Institutional Official, shall promptly provide OPRR with a full explanation of the circumstances and actions taken with respect to:

a. any serious or continuing noncompliance with this Policy;

b. any serious deviation from the provisions of the Guide; or

c. any suspension of an activity by the IACUC.

4. Reports filed under IV.F. of this Policy shall include any minority views filed by members of the IACUC.

# ***Guide for the Care and Use of Laboratory Animals***

Institute of Laboratory Animal Resources  
National Academy Press 1996

Facilities receiving funds from the Public Health Service, National Institutes of Health are obligated to follow the *Guide for the Care and Use of Laboratory Animals*. For the purposes of this publication, references and other notations have been removed. A full-text version of the *Guide* can be found at <http://www.nap.edu/readingroom/books/labrats/contents.html>

## **Chapter 1**

### **INSTITUTIONAL POLICIES AND RESPONSIBILITIES**

Proper care, use, and humane treatment of animals used in research, testing, and education (referred to in this Guide as animal care and use) require scientific and professional judgment based on knowledge of the needs of the animals and the special requirements of the research, testing, and educational programs. The guidelines in this section are intended to aid in developing institutional policies governing the care and use of animals.

Each institution should establish and provide resources for an animal care and use program that is managed in accord with this Guide and in compliance with applicable federal, state, and local laws and regulations, such as the federal Animal Welfare Regulations, or AWRs (CFR 1985), and Public Health Service Policy on Humane Care and Use of Laboratory Animals, or PHS Policy (PHS 1996). To implement the recommendations in this Guide effectively, an institutional animal care and use committee (IACUC) must be established to oversee and evaluate the program.

Responsibility for directing the program is generally given either to a veterinarian with training or experience in laboratory animal science and medicine or to another qualified professional. At least one veterinarian qualified through experience or training in laboratory animal science and medicine or in the species being used must be associated with the program. The institution is responsible for maintaining records of the activities of the IACUC and for conducting an occupational health and safety program.

### **MONITORING THE CARE AND USE OF ANIMALS**

#### **Institutional Animal Care and Use Committee**

The responsible administrative official at each institution must appoint an IACUC, also referred to as "the committee," to oversee and evaluate the institution's animal program, procedures, and facilities to ensure that they are consistent with the recommendations in this Guide, the AWRs, and the PHS Policy. It is the institution's responsibility to provide suitable orientation, background materials, access to appropriate resources, and, if necessary, specific training to assist IACUC members in understanding and evaluating issues brought before the committee.

Committee membership should include the following:

- ★ A doctor of veterinary medicine, who is certified (see American College of Laboratory Animal Medicine, ACLAM, Appendix B) or has training or experience in laboratory animal science and medicine or in the use of the species in question.
- ★ At least one practicing scientist experienced in research involving animals.
- ★ At least one public member to represent general community interests in the proper care and use of animals. Public members should not be laboratory animal users, be affiliated with the institution, or be members of the immediate family of a person who is affiliated with the institution.

The size of the institution and the nature and extent of the research, testing, and educational programs will determine the number of members of the committee and their terms of appointment. Additional information about committee composition can be found in the PHS Policy and the AWRs.

The committee is responsible for oversight and evaluation of the animal care and use program and its components described in this Guide. Its functions include inspection of facilities; evaluation of programs and animal-activity areas; submission of reports to responsible institutional officials; review of proposed uses of animals in research, testing, or education (i.e., protocols); and establishment of a mechanism for receipt and review of concerns involving the care and use of animals at the institution.

The IACUC must meet as often as necessary to fulfill its responsibilities, but it should meet at least once every 6 months. Records of committee meetings and of results of deliberations should be maintained. The committee should review the animal-care program and inspect the animal facilities and activity areas at least once every 6 months. After review and inspection, a written report, signed by a majority of the IACUC, should be made to the responsible administrative officials of the institution on the status of the animal care and use program and other activities as stated herein and as required by federal, state, or local regulations and policies. Protocols should be reviewed in accord with the AWRs, the PHS Policy, *U.S. Government Principles for Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training*, and this Guide.

### **Animal Care and Use Protocols**

The following topics should be considered in the preparation and review of animal care and use protocols:

- ★ Rationale and purpose of the proposed use of animals.
- ★ Justification of the species and number of animals requested. Whenever possible, the number of animals requested should be justified statistically.
- ★ Availability or appropriateness of the use of less-invasive procedures, other species, isolated organ preparation, cell or tissue culture, or computer simulation.
- ★ Adequacy of training and experience of personnel in the procedures used.

- ★ Unusual housing and husbandry requirements.
- ★ Appropriate sedation, analgesia, and anesthesia. (Scales of pain or invasiveness might aid in the preparation and review of protocols.)
- ★ Unnecessary duplication of experiments.
- ★ Conduct of multiple major operative procedures.
- ★ Criteria and process for timely intervention, removal of animals from a study, or euthanasia if painful or stressful outcomes are anticipated.
- ★ Postprocedure care.
- ★ Method of euthanasia or disposition of animal.
- ★ Safety of working environment for personnel.

Occasionally, protocols include procedures that have not been previously encountered or that have the potential to cause pain or distress that cannot be reliably controlled. Such procedures might include physical restraint, multiple major survival surgery, food or fluid restriction, use of adjuvants, use of death as an end point, use of noxious stimuli, skin or corneal irritancy testing, allowance of excessive tumor burden, intracardiac or orbital-sinus blood sampling, or the use of abnormal environmental conditions. Relevant objective information regarding the procedures and the purpose of the study should be sought from the literature, veterinarians, investigators, and others knowledgeable about the effects on animals. If little is known regarding a specific procedure, limited pilot studies designed to assess the effects of the procedure on the animals, conducted under IACUC oversight, might be appropriate. General guidelines for evaluation of some of those methods are provided in this section, but they might not apply in all instances.

## **Physical Restraint**

Physical restraint is the use of manual or mechanical means to limit some or all of an animal's normal movement for the purpose of examination, collection of samples, drug administration, therapy, or experimental manipulation. Animals are restrained for brief periods, usually minutes, in most research applications.

Animals can be physically restrained briefly either manually or with restraint devices. Restraint devices should be suitable in size, design, and operation to minimize discomfort or injury to the animal. Many dogs, nonhuman primates (e.g., Reinhardt 1991, 1995), and other animals can be trained, through use of positive reinforcement, to present limbs or remain immobile for brief procedures.

Prolonged restraint, including chairing of nonhuman primates, should be avoided unless it is essential for achieving research objectives and is approved by the IACUC. Less-restrictive systems that do not limit an animal's ability to make normal postural adjustments, such as the tether system for nonhuman primates and stanchions for farm animals, should be used when compatible with protocol objectives. When restraint devices are used, they should be specifically designed to accomplish research goals that are impossible or impractical to accomplish by other means or to prevent injury to animals or personnel.

The following are important guidelines for restraint:

- ★ Restraint devices are not to be considered normal methods of housing.



- ★ Restraint devices should not be used simply as a convenience in handling or managing animals.
- ★ The period of restraint should be the minimum required to accomplish the research objectives.
- ★ Animals to be placed in restraint devices should be given training to adapt to the equipment and personnel.
- ★ Provision should be made for observation of the animal at appropriate intervals, as determined by the IACUC.
- ★ Veterinary care should be provided if lesions or illnesses associated with restraint are observed. The presence of lesions, illness, or severe behavioral change often necessitates temporary or permanent removal of the animal from restraint.

## **Multiple Major Surgical Procedures**

Major surgery penetrates and exposes a body cavity or produces substantial impairment of physical or physiologic function. Multiple major survival surgical procedures on a single animal are discouraged but may be permitted if scientifically justified by the user and approved by the IACUC. For example, multiple major survival surgical procedures can be justified if they are related components of a research project, if they will conserve scarce animal resources or if they are needed for clinical reasons. If multiple major survival surgery is approved, the IACUC should pay particular attention to animal well-being through continuing evaluation of outcomes. Cost savings alone is not an adequate reason for performing multiple major survival surgical procedures (AWRs).

## **Food or Fluid Restriction**

When experimental situations require food or fluid restriction, at least minimal quantities of food and fluid should be available to provide for development of young animals and to maintain long-term well-being of all animals. Restriction for research purposes should be scientifically justified, and a program should be established to monitor physiologic or behavioral indexes, including criteria (such as weight loss or state of hydration) for temporary or permanent removal of an animal from the experimental protocol. Restriction is typically measured as a percentage of the ad libitum or normal daily intake or as percentage change in an animal's body weight.

Precautions that should be used in cases of fluid restriction to avoid acute or chronic dehydration include daily recording of fluid intake and recording of body weight at least once a week or more often, as might be needed for small animals, such as rodents. Special attention should be given to ensuring that animals consume a suitably balanced diet because food consumption might decrease with fluid restriction. The least restriction that will achieve the scientific objective should be used. In the case of conditioned-response research protocols, use of a highly preferred food or fluid as positive reinforcement, instead of restriction, is recommended. Dietary control for husbandry or clinical purposes is addressed in Chapter 2. (Ed. Note: This is not included in this excerpted version.)

## **VETERINARY CARE**

Adequate veterinary care must be provided, including access to all animals for evaluation of their health and well-being. Institutional mission, programmatic goals, and size of the animal

program will determine the need for full-time, part-time, or consultative veterinary services. Visits by a consulting or part-time veterinarian should be at intervals appropriate to programmatic needs. For specific responsibilities of the veterinarian, see Chapter 3.

Ethical, humane, and scientific considerations sometimes require the use of sedatives, analgesics, or anesthetics in animals. An attending veterinarian (i.e., a veterinarian who has direct or delegated authority) should give research personnel advice that ensures that humane needs are met and are compatible with scientific requirements. The AWRs and PHS Policy require that the attending veterinarian have the authority to oversee the adequacy of other aspects of animal care and use. These can include animal husbandry and nutrition, sanitation practices, zoonosis control, and hazard containment.

## **PERSONNEL QUALIFICATIONS AND TRAINING**

AWRs and PHS Policy require institutions to ensure that people caring for or using animals are qualified to do so. The number and qualifications of personnel required to conduct and support an animal care and use program depend on several factors, including the type and size of institution, the administrative structure for providing adequate animal care, the characteristics of the physical plant, the number and species of animals maintained, and the nature of the research, testing, and educational activities.

Personnel caring for animals should be appropriately trained and the institution should provide for formal or on-the-job training to facilitate effective implementation of the program and humane care and use of animals. According to the programmatic scope, personnel will be required with expertise in other disciplines, such as animal husbandry, administration, laboratory animal medicine and pathology, occupational health and safety, behavioral management, genetic management, and various other aspects of research support.

There are a number of options for the training of technicians. Many states have colleges with accredited programs in veterinary technology (AVMA 1995); most are 2-year programs that result in associate of science degrees, and some are 4-year programs that result in bachelor of science degrees. Nondegree training, with certification programs for laboratory animal technicians and technologists, can be obtained from the American Association for Laboratory Animal Science (AALAS). There are commercially available training materials that are appropriate for self-study. Personnel using or caring for animals should also participate regularly in continuing-education activities relevant to their responsibilities. They are encouraged to be involved in local and national meetings of AALAS and other relevant professional organizations. On-the-job training should be part of every technician's job and should be supplemented with institution-sponsored discussion and training programs and with reference materials applicable to their jobs and the species with which they work. Coordinators of institutional training programs can seek assistance from the Animal Welfare Information Center (AWIC) and ILAR. The Guide to the Care and Use of Experimental Animals by the Canadian Council on Animal Care and guidelines of some other countries are valuable additions to the libraries of laboratory animal scientists.

Investigators, technical personnel, trainees, and visiting investigators who perform animal anesthesia, surgery, or other experimental manipulations must be qualified through training or experience to accomplish these tasks in a humane and scientifically acceptable manner.

## **OCCUPATIONAL HEALTH AND SAFETY OF PERSONNEL**

An occupational health and safety program must be part of the overall animal care and use program. The program must be consistent with federal, state, and local regulations and should focus on maintaining a safe and healthy workplace. The program will depend on the facility, research activities, hazards, and animal species involved. The National Research Council publication *Occupational Health and Safety in the Care and Use of Research Animals* contains guidelines and references for establishing and maintaining an effective, comprehensive program. An effective program relies on strong administrative support and interactions among several institutional functions or activities, including the research program (as represented by the investigator), the animal care and use program (as represented by the veterinarian and the IACUC), the environmental health and safety program, occupational-health services, and administration (e.g., human resources, finance, and facility-maintenance personnel). Operational and day-to-day responsibility for safety in the workplace, however, resides with the laboratory or facility supervisor (e.g., principal investigator, facility director, or veterinarian) and depends on performance of safe work practices by all employees.

# Agency Directives for Federal Fund-holders







# United States Department of Agriculture Research, Education, and Economics

ARS □ CSREES □ ERS □ NASS

## *Policies and Procedures*

This document is available at <http://www.afm.ars.usda.gov/ppweb/>

Title: Animal Care and Use Committee

Number: 130.4

Date: 8/29/90

Originating Office: Office of the Deputy Administrator, National Program Staff

This Replaces: Remove AM 130-4 Dated 6/1/77

Distribution: Headquarters, Areas, and Locations

This Directive states policy, responsibilities, committee membership, committee procedures, including reporting requirements for IACUCs.

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## 1. Reference

For definitions of terms, regulations, animal coverage, and standards of care and use, see DIRECTIVE 635.1, Humane Animal Care and Use.

## 2. Summary

The amended Animal Welfare Act (AWA) regulations contained in 9 CFR Part 2, Subpart 2C, Section 2.37 (see Exhibit 1) require each Federal research facility that uses animals to establish an Institutional Animal Care and Use Committee (IACUC). Locations that receive extramural funds from the Public Health Service (PHS) for studies that use animals in biomedical research and testing require an IACUC. The specific requirements set forth by the AWA and PHS Policy are not identical.

It is ARS Policy for (a) all ARS Locations using ARS funds, personnel, or physical resources; (b) all non-ARS locations using either ARS funds, personnel or animals; or (c) ARS personnel using funds from non-ARS sources and engaging in research and testing that use vertebrate animals to have an IACUC. Although AWA legislation specifically excludes from AWA overview farm animals used or intended for use as food or fiber, or when used or intended for use in agricultural research, it is ARS Policy to include overview of all ARS vertebrate animals by IACUCs at ARS Locations or at non-ARS locations. It is also ARS Policy to include overview by ARS IACUCs of non-ARS animals at ARS Locations or non-ARS locations using either ARS funds or personnel.

The ARS Policy described herein fulfills the requirements of both the AWA and PHS Policy.

This Directive states policy, responsibilities, committee membership, committee procedures, including reporting requirements for IACUCs.

### 3. Abbreviations

AALAS -	American Association for Laboratory Animal Science
AD -	Area Director
Ag Guide -	Guide for the Care and Use of Agricultural Animals in Agricultural Research and Teaching
APHIS-	Animal and Plant Health Inspection Service
AWA -	Animal Welfare Act
CD -	Center Director
CAD -	Contracting and Assistance Division
CRIS -	Current Research Information System
CFR -	Code of Federal Regulations
IACUC-	Institutional Animal Care and Use Committee
LERB -	Labor and Employee Relations Branch, Personnel Division, ARS
NIH -	National Institutes of Health
NIH Guide -	NIH Guide for the Care and Use of Laboratory Animals
NPS -	National Program Staff
OPRR -	Office for the Protection from Research Risks, NIH
PD -	Personnel Division
PHS -	Public Health Service
PI -	Principal Investigator
PL -	Public Law
REAC -	Regulatory Enforcement Animal Care, APHIS
VS -	Veterinary Services, APHIS

### 4. Definitions

Activity. Each unique, related series of procedures done on an animal or group of animals addressed in a single Protocol Form.

Protocol Form. The form that contains descriptions of animal care and use activities for which IACUC approval is requested by the PI. Points which must be addressed in the Protocol Form are described in AWA, 9 CFR, Subpart 2C, Section 2.31[d] (see Exhibit 1).

Cooperator. AB used in this Directive, taken to mean any non-ARS personnel caring for or using any vertebrate animal at an ARS Location.

### 5. Forms

VS Form 18-1, USDA Interstate and International Certificate of Health Examination for Small Animals. See Exhibit 2 for model form. This form and other VS forms can be obtained from Sector Supervisor, REAC, APHIS at the addresses listed.

VS Form 18-5, Record of Dogs and Cats on Hand. See Exhibit 2 for model form.



VS Form 18-6, Record of Disposition of Dogs and Cats. See Exhibit 2 for model form.

APHIS Form 7008 (Replaces Form VS Form 18-8), Inspection of Animal Facilities, Sites or Premises. The numbers on the refer to AWA, Standards section of 9 CFR 3. Obtain forms from REAC/APHIS. See Exhibit 2 for model Form and APHIS addresses.

VS Form 18-23, Annual Report of Research Facilities. Obtain Forms from REAC/APHIS. See Exhibit 2 for model Form and APHIS addresses.

ARS Form 605, Annual Report of Farm Animals Used in Agricultural Research (Exhibit 3).

ARS Form 606, IACUC Membership (Exhibit 3).

## 6. Authorities

- Laboratory Animal Welfare Act of 1966 (PL 89-544) as amended by the Animal Welfare Act of 1970 (PL 91-579); 1976 (PL 94-279); and 1985 (PL 99-198).
- 9 CFR 1, 2 (Subpart 2C), and 3.
- Health Research Extension Act, Section 495 (Animals in Research) (PL 99-158). PHS Policy on Humane Care and Use of Laboratory Animals as revised 1986 and the NIH Guide for the Care and Use of Laboratory Animals, revised 1985 (NIH Publication 86-23).
- Guide for the Care and Use of Agricultural Animals in Agricultural Research and Teaching, First Edition 1988 (Chapters 5-11). Also referred to as Ag Guide in this Directive.
- Interagency Research Animal Committee's U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training, Federal Register, May 20, 1985, V. 50, No. 97 (Exhibit 4).

## 7. Coverage

Use of all vertebrate animals for any purpose used at either any ARS Location, regardless of source of funds, or at another location using ARS funds or ARS personnel regardless of source of funds.

## 8. Policy

It is ARS policy:

To include all vertebrate animals used at either any ARS Location, regardless of source of funds, or at another location using ARS funds or ARS personnel regardless of source of funds under the IACUC overview provisions outlined in 9 CFR Part 2C (AWA). Further, the constitution of these IACUCs will conform to minimum membership and distribution characteristics stated in PHS Policy

(i.e., at least five members). This statement formalizes Memoranda from ARS Administrator 1986, 1987, 1988, and 1989.

That all ARS Locations using vertebrate animals or other locations using ARS animals, personnel or funds for supporting any vertebrate animal use and also receive funds from any PHS agency, conform to the assurance requirements set out in PHS Policy Guidelines.

## 9. Responsibilities

The Administrator through the NPS administers the program and assures regulations and standards are enforced.

The AD's assure:

- IACUCs are established where required. b Regulations and standards are enforced.
- Members and chairpeople of IACUCs are appointed.
- That noncompliances with ARS Policy, AWA, NIH Guide, and Ag Guide are corrected/resolved in a timely manner. Further, when warranted, cases involving animal abuse should be referred to LERB (when ARS employees are involved) or to CAD (when cooperator employees are involved) for a determination of the appropriateness of disciplinary or remedial actions.
- Review of reports to assure regulations, standards, and policies are enforced and then certify accuracy of reports. Transmit annual reports to REAC/APHIS (see Exhibit 2 for addresses), OPRR/NIH (when necessary), and NPS.
- Provision of consultation and guidance deemed necessary under AWA and ARS Policy.
- Upon request of APHIS representative, information required under the AWA is furnished. For ARS Locations receiving PHS funds, upon request of OPRR/NIH representative, information required under PHS Policy is furnished.
- Deficiencies in animal facilities are corrected promptly.

The IACUC:

- Reviews and approves or disapproves all proposed activities for use of animal subjects (commonly known as "Protocol Review-"); maintains a record of these reviews and also transmits the results of such reviews to the PI and Location's highest management official (if other than AD). This review shall conform to the standards set forth in AWA, 9 CFR 2C, Section 2.31.

NOTE: Proposed animal use activities that have been approved by the IACUC may be subject to further review by CD or AD or NPS. However, these officials cannot

approve sections of a proposal related to the care and use of animals if they have not been approved previously by the IACUC.

- Monitors animal use activities through Protocol Form review and facility inspections to assure that once an experimental procedure has been approved, no substantial change is made unless a formal request (amended Protocol Form) with appropriate justification is submitted to the IACUC and approved.
- Conducts annual review of all activities for use of animal subjects that exceed periods longer than 1 year and approve continuation or suspend approval. File maintenance and transmission of results of Protocol Form review are as stipulated in I.3.a (above).
- At irregular intervals, dictated by complaint of nonconformance to the stipulations in an approved activity or request from PI for approval of change in an approved activity, reviews an animal use activity. All requested changes must be approved by the IACUC before the activity proceeds. Investigations of complaints are addressed in paragraph I.3.e (below). File maintenance and transmission of results of review are as stipulated above.
- Promptly investigate all complaints concerning abuse of animals, nonconformance with stipulations of an approved activity, or failure to comply with provisions of the AWA, NIH Guide, Ag Guide, and ARS Directives concerning care and use of animals. If warranted after investigation of complaints, recommend to the AD a course of corrective action including, but not limited to, referral to LERB (when ARS employees are involved) or CAD (when cooperator employees are involved) to determine whether formal investigation concerning possible disciplinary action is warranted regarding any employee or cooperator found to have abused animals.
- Review, at least every 6 months, the location's program for humane care and use of animals using AWA 9 CFR Subpart 2C, the NIH Guide, and the Ag Guide as bases for evaluation. -
- Inspect, at least every 6 months, all of the locations' and tenant agencies' animal facilities, including satellite facilities and other study areas (defined as "any building, room, area, enclosure, or other containment outside of the centrally designated or managed area") in which animals are held for more than 12 hours. The NIH Guide, Ag Guide, and AWA 9 CFR Subpart 2C are used as bases for evaluation.
- Prepare semiannual reports of IACUC evaluations for the AD. These reports must contain a description of any major deviations (and reasons for such deviations) from the requirements outlined in AWA 9 CFR Subpart 2C, PHS Policy (where relevant) and the Ag Guide. In cases of major deviations, the IACUC Chair and attending veterinarian should immediately suspend the problem activity, report to AD, and request immediate correction of the problem or, if not possible, terminate the problem-causing activity.
- In consultation with PD, procure, develop, or recommend to AD sources of training in humane care and use of animals and regulatory overview for ARS employees,

including those not directly involved with animal care and use. The attending veterinarian member of the IACUC has the specific responsibility for assuring that animal surgery, pre- and post-surgical care, and appropriate methods of euthanasia comply with currently accepted veterinary practices.

- Maintain files documenting IACUC membership, animal facility inspections, reports to AD, Protocol Form reviews, and IACUC meeting minutes for at least 3 years.

## 10. Committee Membership

Consists of at least:

One Doctor of Veterinary Medicine, with training or experience with the care of the species in residence at the Location and who has direct or delegated program responsibility for activities involving animals at the Location.

One scientist experienced, and currently active, in research involving animals.

One member whose primary concerns are in a nonscientific area (e.g. ethicist, attorney, business person, clergy etc.).

One individual who is not affiliated with the institution in any way other than as a member of the IACUC and is not a member of the immediate family or a person who is affiliated with the institution.

NOTE: Furthermore, an individual who meets the requirements of more than one of the above categories may fulfill more than one requirement. However, no IACUC may have fewer than 5 members.

It is strongly recommended that all ARS IACUCs include, in addition to a senior scientist, an animal technician or caretaker.

Rotation of IACUC membership is encouraged.

## 11. IACUC Officers and Duties

Chairperson:

- Calls meetings as often as required for timely reviews of animal care and use protocol forms and other business. Meetings must be called at least semiannually.
- Assures that IACUC activities meet regulatory requirements. c Develops and submits reports to AD.
- On own initiative, or upon request of the IACUC, makes recommendations to AD on any aspect of humane care and use of animals.



- Promptly leads investigation of allegations of animal abuse. Reports results of investigations to the AD and, if warranted, recommends a course of corrective action including, but not limited to, referral to LERB to determine whether formal investigation concerning possible disciplinary action is warranted regarding any employee found to have abused animals or to CAD concerning a cooperator found to have abused animals. f Maintains the official IACUC file.

#### Secretary:

- Records minutes at IACUC meetings.
- Prepares the reports developed by the IACUC chairperson.
- Maintains file of IACUC members and any secondary files agreed upon by the ARS Location's management.
- Sends out IACUC meeting notices, draft minutes, and meeting agendas to IACUC members in a timely manner.

## **12. IACUC Meetings**

- Held at least semiannually for business other than Protocol Form review. Meetings must be held after each semiannual facility inspection so that the results can be reviewed by a quorum of the IACUC members and recommendations concerning those inspections developed for transmission to the AD.
- Protocol Form review meetings must be held with a frequency that assures timely transmission of results of the review to the PI. The AWA allows Protocol Form review by a subcommittee as long as: (a) all members of the IACUC receive a complete list of all Protocol Forms to be reviewed and (b) any member of the IACUC can request review of the animal care and use Protocol Forms by the full IACUC. Any minority votes on a Protocol Form review must be recorded along with the grounds for the vote.
- Written records of IACUC meetings must be made and kept for 3 years.

## **13. Reports**

#### Attending Veterinarian

On or before November 15 of each year, prepare original and three copies of VS Forms 18-5, 18-6, and 18-23 and ARS 605 covering the previous fiscal year ending September 30 and transmit the signed documents to IACUC secretary.

## Secretary IACUC

On or before November 15 of each year, prepare original and three copies of report of activities of IACUC and also prepare IACUC membership form (ARS 606).

Only for locations that receive PHS funds and, therefore, have filed an Assurance with OPRR/NIH~ annually on or before December 1, prepare original and three copies of the annual report stipulated by PHS Policy.

Distribute documents: Original and two copies to AD.

Retain documents: Retain one copy for file.

NOTE: Discard copies after 3 years.

## AD

When documents are received, review for accuracy and compliance with ARS, AWA, and PHS policy. Accuracy is certified by AD signature.

Distribute documents:

- Original certified copy of VS Form 18-23 to Sector Supervisor, REAC, APHIS (See Exhibit 2 for addresses).
- Original certified copy of PHS Annual Assurance Report to OPRR/NIH, Building 31, Room 5B59, Bethesda, Maryland 20892.
- One certified copy of the reports listed in M1, M2 [a list of all members of the IACUC along with their offices (if any) in the IACUC, highest academic degree, inclusive term of membership on the IACUC, official ARS title, and complete mailing address and telephone number (including area code)] and M3 (for Locations that receive PHS funds) to NPS Animal Care Office, BARC-West, Beltsville, Maryland 20705.

Retain: One certified copy for file.

NOTE: Discard copies after 3 years.

**R. D. PLOWMAN**  
**Administrator**

# United States Department of Agriculture Research, Education, and Economics

ARS □ CSREES □ ERS □ NASS

## *Policies and Procedures*

This document is available at <http://www.afm.ars.usda.gov/ppweb/>

**Title:** Humane Animal Care and Use

**Number:** 635.1

**Date:** 8/29/90

**Originating Office:** Office of the Deputy Administrator National Program Staff

**This Replaces:** AM 535 dated 6/1/77

**Distribution:** ARS Headquarters, Areas, and Locations

This Directive states:  
ARS Policy; lists coverage of  
animals under Public Laws,  
Policies and ARS practices; and  
assigns responsibilities for  
assuring humane animal care and  
use.

# Table Of Contents

1. References
2. Abbreviations
3. Definition
4. Coverage
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6. Policy
7. Licensing and Registration
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## 1. References

For additional information see DIRECTIVE 130.4, Animal Care and Use Committee.

## 2. Abbreviations

AALAS	-	American Association for Laboratory Animal Science
AD	-	Area Director
AV	-	Attending Veterinarian
AWA	-	Animal Welfare Act
APHIS	-	Animal and Plant Health Inspection Service, USDA
CFR	-	Code of Federal Regulations
Ag Guide	-	Guide for the Care and Use of Agricultural Animals in Agricultural Research and Teaching
IACUC	-	Institutional Animal Care and Use Committee
LERB	-	Labor and Employee Relations Branch, Personnel
PL	-	Public Law
REAC	-	Regulatory Enforcement Animal Care, APHIS
RL	-	Research Leader (ARS)
SY	-	Research Scientist (ARS)
VS	-	Veterinary Services, APHIS

## 3. Definition

Cooperator . As used in this Directive, taken to mean any non-ARS personnel caring for or using any vertebrate animal at an ARS Location.



## 4. Coverage

### 1. ARS Policy:

- a. Includes: All vertebrate animals in all ARS Locations, or other locations in which ARS funds or ARS personnel are involved.
- b. Excludes: Invertebrate animals.

### 2. AWA:

- a. Includes: Any live or dead dog, cat, nonhuman primate, guinea pig, hamster, rabbit, or any other warmblooded animal, used or intended for use in research, teaching, testing, experimentation, or exhibition purposes, or as a pet.
- b. Excludes: Birds, rats of the genus *Rattus* and mice of the genus *Mus* bred for use in research, and horses and other farm animals, such as, but not limited to livestock and **poultry used** or intended for use as food or fiber, or livestock or poultry used or intended for use for improving animal nutrition, breeding, management, or production efficiency, or for improving the quality of food or fiber.

### 3. PHS Policy:

- a. Includes: Any animal (including farm animals) used in biomedical research and testing funded by a PHS Agency or in any institution that receives funds from a PHS Agency.
- b. Excludes: Livestock and poultry used or intended for use that also is excluded from coverage by the AWA.

### 4. Ag Guide:

- a. Includes: Livestock and poultry used in agricultural research and teaching.
- b. Excludes: Animals covered by AWA or PHS.

## 5. Authorities

- Laboratory Animal Welfare Act of 1966 as amended by the Animal Welfare Act of 1970, 1976 and 1985.
- 9 CFR 11.2 (Subpart 20, and 3).
- U.S. PHS Policy on Humane Care and Use of Laboratory Animals, 1986 revision.
- NIH Guide for the Care and Use of Laboratory Animals, 1985 revision (NIH Publication No. 86-23).

- Guide for the Care and Use of Agricultural Animals in Agricultural Research and Teaching, First Edition March, 1988.

## 6. Policy

It is ARS policy to assure that all ARS research animals are treated humanely. Allegations of animal abuse must be reported promptly, in writing, to the Chairperson, IACUC, and the AD. It is ARS Policy to assure that all ARS research facilities and other facilities using ARS animals, funds or personnel for any animal use comply with the following:

1. The AWA, for animals used in biomedical research, testing or teaching and covered by the AWA including:
  - a. The AWA, its amendments, regulations, and standards concerning procurement, transportation, care, handling, and treatment of animals, training of personnel, and employee health programs (Exhibit 1).
  - b. Requirement to maintain IACUCs in all ARS Locations that have animals covered by the AWA (except that ARS requires a minimum of five members whereas AWA requires a minimum of three). See also Directive 130.4, Animal Care and Use Committee.
  - c. Assurance that animals not covered under the AWA receive the same level of humane animal care and treatment.
  - d. Review, and, if warranted, investigate concerns involving care and use of animals resulting from complaints or reports of noncompliance.
2. PHS Policy, for ARS facilities receiving funds from any PHS agency including:
  - a. "PHS Policy, and also NIH Guide concerning procurement, transportation, care, handling, and treatment of animals, training of personnel, and employee health programs (Exhibit 2).
  - b. Maintain IACUCs that comply with PHS Policy in all ARS Locations that use animals. Note that ARS and PHS Policy concerning IACUC size and composition are identical. See also Directive 130.4, Animal Care and Use Committee.
  - c. Assurance that animals not covered under PHS Policy receive the same level of humane animal care and treatment.
3. Ag Guide, for ARS facilities or facilities receiving ARS funds and using farm animals for any purpose with the following stipulations:
 

Ag Guide chapters 5-11 outlining appropriate husbandry practices for various species of farm animals (Exhibit 3).

## 7. Licensing and Registration

1. Not required for Federal agencies under the AWA.
2. Filing of an annual PHS Assurance with OPRR/NIH is required for all ARS Locations that receive funds from any PHS agency. Many other public and private funding entities also require filing of a PHS Assurance as a condition of grant/contract completion.

## 8. Responsibilities

1. The Administrator, where applicable, through the NPS, assures compliance with ANA, PHS Policy and NIH Guide, Ag Guide, and ARS Policy concerning humane care and use of all vertebrate \1-1/ animals.
2. AD's assure:
  - a. IACUCs are established where required and maintained in operation.
  - b. IACUC members and Chairpeople are appointed and function according to Directive 130.4, Animal Care and Use Committee.
  - c. That all employees who work with animals are appropriately trained.
  - d. Regulations, standards, and policies are enforced.
  - e. Reporting requirements for AWA, PHS Policy (where applicable), and ARS are met in a timely manner.
  - f. Deficiencies, including those involving physical facilities, are corrected promptly.
  - g. Procurement of all vertebrate animals in Areas/Centers/Locations is covered by an IACUC approval for the stipulated number of animals.
  - h. Consultation to IACUC, Attending Veterinarians, and/or other employees concerning animal care and welfare is provided.
  - i. That upon request of APHIS representatives, information required under the AWA is furnished.
  - j. That, if needed, assistance is requested from APHIS and/or OPRR/NIH concerning attainment of policy goals.
  - k. Funds and time are provided for employees to receive training required under the AWA.
1. Reported noncompliances with ARS Policy, the AWA and/or PHS Policy are investigated promptly and resolved.

- m. That prompt disciplinary action is taken regarding any employee or cooperator found to have abused animals.
3. Area/Center/Location Procurement Officer and Area/Center Location Property Office will assure that all orders for acquisition and disposition of all vertebrate animals comply with the AWA and ARS Directives concerning approved sources, and assurance that appropriate documentation accompanies all acquisitions and dispositions of animals.
4. RLs/SYs assure:
- a. Acquisition of all animals comply with the AWA and ARS Policy.
  - b. Recordkeeping complies with the AWA, including the special recordkeeping required for dogs and cats that is described in Subpart 2C, Section 2.35.
  - c. Compliance with all special requirements concerning dogs and cats (Directive 130.4, Animal Care and Use Committee) that are delegated to RLs/SYs.
  - d. Dogs and cats obtained from sources other than dealers, exhibitors, and exempt persons are held for at least 5 full days before they are used.
  - e. All animals held or used for any purpose are covered by IACUC approval.
  - f. Recordkeeping provisions of the AWA, Subpart 2C, Section 2.35 concerning dogs and cats are followed and forms/records are forwarded to the appropriate Area IACUC (the official Area Record).
  - g. They personally, as well as their technicians, caretakers, students, and others are aware of and follow regulations and standards for humane care of animals used in any manner by them and/or their subordinates.
  - h. Any inadequacies in care, handling, or environmental conditions concerning animals are promptly reported and corrected.
  - i. Maintenance of training on regulatory requirements and humane care and use of animals.
  - j. Disposition of all healthy surplus animals comply with ARS property disposal procedures for disposition of surplus government animals. In addition, disposition of all dogs and cats also must comply with the AWA concerning recordkeeping (Subpart 2C, Section 2.35), euthanasia, sale, or transportation.
5. Attending Veterinarian:
- a. Serves on the IACUC
  - b. Assures that:



- i. All vertebrate animals receive adequate veterinary care in compliance with the AWA, NIH Guide, and Ag Guide.
  - ii. Guidance is provided to appropriate research and care personnel concerning, including but not limited to, care and use of animals regarding humane handling, immobilization, anesthesia, analgesia, euthanasia, tranquilization, as well as pre-and post-procedural care in accordance with established veterinary and nursing procedures and the AWA.
  - iii. VS Form 18-23 covering the previous fiscal year ending September 30 is accurately completed, receives concurrence by IACUC, and forwarded to AD for transmission to REAC/APHIS and NPS/ARS in a timely manner.
  - iv. ARS Form 605 covering the previous fiscal year ending September 30 is accurately completed, receives concurrence by IACUC, and forwarded to AD for transmission to NPS/ARS in a timely manner.
  - v. Animal caretakers receive an adequate level of training to provide optimum care of animals.
  - vi. Chairperson, IACUC, RL, Center Director, and AD are promptly notified about all failures to comply with provisions of AWA, NIH Guide, and Ag Guide concerning regulations and standards.
  - vii. Knowledge of new veterinary medical developments and regulatory requirements is maintained through a continuing program of training.
6. Consulting Veterinarian assume same responsibilities as attending veterinarian.
7. Animal Caretakers assure:
- a. All animals under their responsibility receive care consistent with the AWA, NIH Guide, and Ag Guide on a daily basis, except for free ranging animals where Location IACUCs set the appropriate frequency.
  - b. All management and environmental requirements for animals are met in a timely manner.
  - c. Maintenance of current knowledge of all aspects of care for the species in their charge through a continuing program of training.
  - d. That during the first year of employment as animal caretaker, they take a course leading to certification given by AALAS (for laboratory animal caretakers) or by another organization/institution (for caretakers of species for which AALAS training is inappropriate). This course must contain training in current animal care practices and regulatory requirements relevant to the species in use. Lists of appropriate training courses leading to employee certification may be obtained from the IACUC. Employee certifications will be updated periodically to assure that they reflect current animal care practices, regulatory requirements, and relevance to the species being cared for.

- e. On or before the first year of employment as animal caretaker, receive certification in the appropriate training course (described in H.7.d above). Failure to meet the certification requirement within a year after entering on duty will be grounds for dismissal.
8. IACUCs will fulfill all of the requirements in Directive 130.4, Animal Care and Use Committee.

R. D. PLOWMAN  
Administrator

**Department of Defense**  
**DIRECTIVE**  
**April 17, 1995**  
**NUMBER 3216.1**

**Use of Laboratory Animals in DoD Programs**

This document may be found at <http://web7.whs.osd.mil/text/d32161p.txt>

References:

(a) DoD Directive 3216.1, "Use of Animals in DoD Programs , " February 1, 1982 (hereby canceled)

(b) Title 9, Code of Federal Regulations, "Animals and Animal Products, " Chapter 1, Subchapter A, "Animal Welfare, " Parts 1, 2, and 3

(c) Public Law 101-511, Department of Defense Appropriations Act for Fiscal Year 1991, Section 8019, Title 10 United States Code, Section 2241

(d) Sections 2131 through 2156 of Title 7, United States Code "The Laboratory Animal Welfare Act of 1966, " as amended

(e) through (f) , see enclosure 1.

**A. REISSUANCE AND PURPOSE**

1. Reissues reference (a) to update policy governing activities using animals within the Department of Defense.

2. Designates the Secretary of the Army as the DoD Executive Agent to develop and issue Service regulations to implement this Directive.

**B. APPLICABILITY**

This Directive applies to the Office of the Secretary of Defense, the Military Departments, the Uniformed Services University of the Health Sciences, and the Defense Agencies (hereafter referred to collectively as "DoD Components") that perform or sponsor activities using animals.

**C. DEFINITIONS**

Terms used in this Directive are defined in enclosure 2.

## **D. DoD POLICY**

1. Federal statutes, regulations, and publications that provide national standards and guidance for the acquisition, transportation, housing, control, maintenance, handling, protection, treatment, care, use, and disposal of animals shall be applicable to all activities using animals. A summary of the applicable documents cited as references is in enclosure 3.
2. Animals shall be legally obtained from suppliers licensed by the U.S. Department of Agriculture (USDA) in accordance with reference (b) unless specifically exempted from the licensing requirements stated in reference (b) .
3. DoD organizations or facilities maintaining animals for use in research, testing or training shall apply for accreditation by the American Association for Accreditation of Laboratory Animal Care (AAALAC) .
4. Alternative methods to animal species shall be considered, whenever possible, if such alternatives produce scientifically valid or equivalent results to attain the research testing and training objectives.
5. The purchase or use of dogs, cats, or nonhuman primates in research conducted for developing biological, chemical or nuclear weapons is prohibited.
6. The purchase or use of dogs, cats, or nonhuman primates for inflicting wounds from any type of weapon(s) to conduct training in surgical or other medical treatment procedures is prohibited. (reference (c)).
7. DoD organizations or facilities wishing to hold training programs using animals, such as advanced trauma life support (ATLS) training programs, shall have the training protocol reviewed and approved by a duly constituted Institutional Animal Care and Use Committee (IACUC) in accordance with references (d) u and (e) and paragraph D.8. of this Directive to ensure the humane use of animals. DoD organizations or facilities conducting ATLS training that require housing of animals for short periods of time shall ensure adequate care and shall have the animal housing facilities inspected and approved by a veterinarian prior to receipt of the animals.
8. All proposals or protocols for animal experiments or demonstrations in RDT&E, clinical investigation, instructional, or training programs conducted or sponsored by a DoD organization or facility shall be reviewed and approved by a duly constituted IACUC composed of a minimum of five members. There shall be at least one non-scientific member on each IACUC. In addition, there also shall be a member who represents the general community interest and is non-affiliated with the facility sponsoring IACUC. The non-affiliated and the non-scientific membership can be filled by the same person. To ensure community representation at each meeting and inspection, an alternate to the non-affiliated member shall be designated for IACUCS having a single non-affiliated membership. Since the DoD IACUCS perform a Government function in an approval process and do not serve merely as an advisory body, the non-affiliated and the non-scientific member(s) to DoD IACUCS shall either be a Federal employee, with demonstrated commitment to the community or a consultant consistent with the requirements established by reference (f) .



9. A headquarters-level administrative review shall be conducted for proposals involving the use of non-human primates conducted or sponsored by subordinate activities of the DoD Component for conformance with all applicable Federal regulations and policies. A DoD component may delegate this responsibility to another DoD component for purposes of efficiency and consolidation of functional offices.
10. The DoD Components shall coordinate and cooperate in the transfer of Government-owned nonhuman primates between facilities to maximize conservation and proper utilization.
11. Proposals intending to use chimpanzees must be further reviewed and approved by the Interagency Animal Model Committee, which coordinates national priorities for research utilization of this species.
12. The DoD components that sponsor animal based research, testing, and training under a DoD grant or contract shall ensure that:
- a. all extramural research proposals using live animals shall be administratively reviewed by a DoD veterinarian trained or experienced in laboratory animal science and medicine before grant or contract award.
  - b. the most recent USDA inspection reports are provided or obtained for the facility under consideration for a research contract or grant using animals, and that during the term of the award, the most recent USDA inspection reports be reviewed on an annual basis.
  - c. a DoD veterinarian trained or experienced in laboratory animal science and medicine shall conduct an initial site visit to evaluate animal care and use programs at contracted facilities conducting DoD-sponsored research using non-human primates, marine mammals, dogs, cats, or proposals deemed to warrant review. The initial site visit shall occur within 6 months of when the facility has taken delivery of the animals under DoD contract or grant award. Any facility receiving a DoD-funded grant or contract for animal based research shall notify the DoD component sponsor and shall have a site inspection within 30 days of notification of loss of AAALAC accreditation for cause, or notification that the facility is under USDA investigation. Site inspections for cause shall evaluate and ensure the adequacy of animal care and use in DoD-sponsored programs, and provide recommendations to the sponsoring DoD component about continued funding support of the research.
13. In the case of differences between the standards of care and use of animals as cited in enclosure 3, the most stringent standard shall apply.
14. Activities covered by this Directive that are performed or sponsored in foreign countries shall be conducted in accordance with applicable U.S. statutory requirements, and regulations and standards of the host country. If differences exist between U.S. and host country regulations or standards, unless prohibited by the host country, the more stringent standard shall apply.
15. While not specifically addressed in this Directive, ceremonial, recreational, and working animals, such as military working dogs, shall be treated in a humane manner.

16. Personnel with complaints of violation of this directive shall report such violations to either of the following members of the organization or facility: IACUC chairperson, attending veterinarian, the facility Commander, or Inspector General. The IACUC shall review and, if warranted, investigate all reports of complaints of animal use or noncompliance with 7 U.S.C. 2131-2 of reference (d), applicable Directives, and regulations.

## **E. RESPONSIBILITIES**

1. The Director, Defense, Research and Engineering (under the Under Secretary of Defense for Acquisition and Technology) or designee shall:

- a. Issue policy and procedural guidance concerning animal use consistent with all applicable Federal regulations and policies.
- b. Designate a DoD representative to the Interagency Research Animal Committee who is a veterinarian of appropriate rank or grade and experience, and preferably also a diplomate of the American College of Laboratory Animal Medicine.
- c. Establish the Joint Technical Working Group (JTWG) to act as the central advisory committee to the Armed Services Biomedical Research Evaluation and Management (ASBREM) Committee on all matters on the care and use of animals for research, testing, clinical investigation, or training within the Department of Defense. The co-chairpersons of the ASBREM Committee shall designate the chairperson of JTWG.

2. The Heads of the DoD Components shall:

- a. Establish appropriate mechanisms to monitor compliance with this Directive and applicable Federal statutes and regulations.
- b. Establish offices or facilities that shall serve as reviewing or approving authorities of animal use proposals from subordinate activities and extramural facilities proposing research under contract or grant.
- c. Provide members to JTWG as required.
- d. Designate the appropriate office(s) within the DoD Component that shall perform the headquarters level administrative review of proposals requiring the use of non-human primates and shall serve as the office where exemptions under paragraph D.2. above may be approved.
- e. Support, and as necessary, ensure the development of animal care and use training programs for researchers and members of the IACUC, and certification programs for all personnel involved in the care, use, and treatment of animals.

3. The Secretary of the Army shall:

- a. As Executive Agent, develop and issue, in consultation with the other DoD Components, joint Service regulations to implement this Directive.

b. Designate the Commander, U.S. Army Veterinary Command/Director, DoD Veterinary Services Activity, a Field Operating Agency of the Army, Office of the Surgeon General who shall serve as a consultant to the Assistant Secretary of Defense for Health Affairs and the Director, Defense Research and Engineering for technical and professional matters related to this Directive.

## F. EFFECTIVE DATE

This Directive is effective immediately.

Enclosures - 3

1. References
2. Definitions
3. Guidance Documents

John M. Deutch

Deputy Secretary of Defense

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April 17, 1995

**3216.1 Enclosure 1**

- (e) National Institutes of Health (NIH) Publication  
No. 86-23, "Guide for the Care and Use of Laboratory  
Animals", United States Department of Health and Human  
Services, National Institutes of Health, Revised 1985.  
(f) Title 5, United States Code, Section 3109.
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Apr 17, 95

3216.1 (Encl 2)

## DEFINITION OF TERMS

1. **Animal**- Any dog, cat, non-human primate, guinea pig, hamster, rabbit or any other live vertebrate animal, which is being used or is intended for use for research, training, testing, or experimentation purposes. For this Directive, it includes birds, rats of the genus *Rattus* and mice of the genus *Mus* bred for use in research, training, testing or experimentation purposes. The term excludes animals used for ceremonial or recreational purposes, military working animals, and animals intended for use as livestock and poultry as food or fiber; or, livestock or poultry used or intended for use for improving animal nutrition, breeding, management, or production efficiency, or for improving the quality of food or fiber.

2. **Clinical Investigation**- All activities directed towards clinical research conducted principally within medical treatment facilities. The Clinical Investigations program is part of the Defense Health Program of the Assistant Secretary of Defense (Health Affairs) and is supported by Major Force Program 8 (MFP-8) funds.

3. **Instructional Program**- All educational and training activities, except training of ceremonial and recreational animals and training associated with military working animals or survival skills training.

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4. **Research, Development, Test, and Evaluation-** All activities which form the RDT&E program of the Director, Defense Research and Engineering (DDR&E) and are supported by Major Force Program 6 (MFP-6) funds.

5. **Alternatives-** Any system or method that covers one or more of the following: replacing or reducing the number of laboratory animals required for an investigation by computer simulation, cell culture techniques, etc; or, refining an existing procedure or technique to minimize the level of stress endured by the animal.

6. **DoD Sponsored Programs.** - All proposals or designs for animal experiments or demonstration in RDT&E, clinical investigation, or instructional programs conducted or funded by grant, award, loan, contract, or cooperative research and development agreement (CRADA).

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Apr 17, 1995  
3216.1 (Encl 3)

### **ADDITIONAL FEDERAL STATUTES , REGULATIONS, AND GUIDELINES ON THE USE OF ANIMALS**

The following documents provide national standards and guidance for the protection, treatment and use of animals:

a. **Animal Welfare Act** (Title 7, United States Code, Sections 2131-2158, as amended, and Title 9, Code of Federal Regulations, Parts 1-4, implementing rules and regulations) . Administered by Regulatory Enforcement and Animal Care (REAC), Animal and Plant Health Inspection Service (APHIS) of the Department of Agriculture. Requires licensing of dealers, identification of animals, maintenance of records, submission of reports, establishment of an Institutional Animal Care and Use Committee (IACUC), and compliance with standards for the humane handling, care, treatment, and transportation of animals by dealers and research facilities.

b. **Endangered Species Act** of 1973 (Title 16, United States Code, Sections 1531-1543, as amended, and Title 50, Code of Federal Regulations, Parts 10-14 and 217-227, implementing rules and regulations) . Provides a program under the U.S. Fish and Wildlife Service, Department of Interior, for conserving threatened and endangered species. Requires import/export - permits, maintenance of records, and submission of reports on the care and handling of endangered, threatened, and conserved species.

c. **Marine Mammal Protection Act** (Title 16, United States Code, Sections 1361-1384, as amended, and Title 50, Code of Federal Regulations, Parts 10-14 and 216-227, implementing rules and regulations) . Provides a program under the Departments of Commerce (National Marine Fisheries Service) and Interior (U.S. Fish and Wildlife Service) for the protection of marine mammals and marine mammal products. Requires acquisition permits, maintenance of records, submission of reports, and inspections on the care and handling of marine mammals.



d. **Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES)** (TIAS 8249, as amended, and Title 50, Code of Federal Regulations, Part 23, implementing rules and regulations) . CITES is a treaty involving 106 signatory nations administered in the United States by the Fish and Wildlife Service of the Department of the Interior. CITES regulates the import and export of imperiled species covered by the treaty but imposes no restrictions or control on interstate shipments.

e. **Lacey Act** (Title 18, United States Code, Section 42, as amended, and Title 50, Code of Federal Regulations, Part 16 and Subpart B, implementing rules and regulations) . A program under the U.S. Fish and Wildlife Service, Department of the Interior. Prohibits the importation of certain wild animals or their eggs if the Secretary of the Interior determines that they are injurious to humans, the interest of agriculture, or other specified national interests.

f. **Guide for the Care and Use of Laboratory Animals.** Public Health Service, National Institutes of Health, NIH Publication No. 86-23, Revised. Provides guidelines for institutional policies, husbandry, requirements, veterinary care, and physical plant requirements for programs involving the care and use of laboratory animals.

g. **Guide for the Care and Use of Agricultural Animals in Agricultural Research and Teaching.** Published by the Consortium for Developing a Guide for the Care and Use of Agricultural Animals in Agricultural Research and Teaching, 309 West Clark Street, Champaign, IL 61820, March 1988. Provides guidelines for the care and use of the major agricultural animal species in the United States in research and teaching. [Ed. Note: An updated version of this document is now available from the Federation of Animal Science Societies, 1111 North Dunlap Avenue, Savoy, IL 61874 USA, telephone: (217) 356-3182, fax: (217) 398-4119, e-mail: [fass@assoqh.org](mailto:fass@assoqh.org)

# Department of Veterans Affairs Veterans Health Administration Washington DC 20420

VHA DIRECTIVE 10-95-031

[http://www.emory.edu/va\\_atl/vmu/va/va031.html](http://www.emory.edu/va_atl/vmu/va/va031.html)

April 14, 1994

## **DEPARTMENT OF VETERANS AFFAIRS (VA) RESPONSIBILITY FOR VA-OWNED RESEARCH ANIMALS HOUSED IN NON-VA FACILITIES AND NON-VA-OWNED RESEARCH ANIMALS HOUSED IN VA FACILITIES**

**1. PURPOSE:** The purpose of this Veterans Health Administration (VHA) directive is to make explicit the application of provisions of M-3, Part I, Chapter 12, Animal Subjects in Research, to: (a) animals owned by the Department of Veterans Affairs (VA), but housed in non-VA research facilities, and (b) animals housed in VA facilities, but owned by non-VA entities. This directive will be incorporated into M-3, Part I, Chapter 1 by February, 1995.

**2. BACKGROUND:** In 1992, The United States Department of Agriculture (USDA) informed VA that research animals owned by VA but held in non-VA facilities, were subject to VA oversight by the SAS (Subcommittee on Animal Studies (SAS) of the VA medical center Research and Development (R&D) Committee. In response to these expectations, and similar expectations where converse arrangements for housing non-VA animals in VA housing existed, further clarification to avoid duplication of effort was sought with USDA and Office for Protection from Research Risks (OPRR)/National Institutes of Health (NIH). The policies and procedures announced in this directive are designed to meet VA, USDA, and OPRR requirements with respect to oversight of research animal care and use practices in the situations described.

### **3. POLICY**

- VA medical centers, acting through the SAS, are responsible for ensuring the humane care and treatment of vertebrate animals used or intended for use in laboratory research. This responsibility extends not only to animals owned by VA and housed in VA facilities, but also to those: (1) owned by VA, but housed in non-VA research facilities, and those (2) housed in VA research facilities, but owned by non-VA entities.
- The SAS must fulfill the programmatic responsibilities described in M-3, Part I, Chapter 12; Federal Regulations (9 Code of Federal Regulations (CFR) Ch. 1, Subch. A, "Animal Welfare"); and the Public Health Service (PHS) Policy on the Humane Care and Use of Laboratory Animals. Compliance with the PHS Policy is required of all VA medical centers that receive PHS research funds or have a letter of assurance of compliance with PHS Policy on file with OPRR. This directive calls special attention to:

- (1) Review of research proposals using animals,
  - (2) Oversight of the animal care and use program, and
  - (3) Record keeping for animal use.
- Efforts should be made to avoid duplication of oversight by VA and affiliated organizations without nullifying the responsibilities and obligations contained in M-3, Part I, Chapter 12, the Federal Regulations, and the PHS Policy.

#### 4. ACTION

- a. In situations where animal subjects are moved between the VA medical center and its affiliated institutions for research or care and housing, the VA medical center remains accountable for compliance of the research and the care and housing of all animals that are housed at the VA medical center, or held there temporarily for research.
- b. The semi-annual program review of the Institutional Animal Care and Use Committee (IACUC) of an institution that houses, holds temporarily, or conducts research on VA-owned animals may be accepted by the VA medical center provided that the report is submitted to and accepted by the SAS of the VA medical center for the responsible Institutional Official (medical center Director) of the VA medical center. Such reports must be held by the VA medical center and acted upon in accordance with the IACUC findings.
- c. When desirable or feasible, a VA medical center and its affiliated institution may have a joint SAS (or IACUC), provided that the appointment of the committee members is concurred in by the VA medical center responsible Institutional Official, has representation from the VA medical center, and is accountable to the VA medical center Institutional Official. In such cases it is recommended that joint committees have responsibility to the VA medical center and the affiliated institution.
- d. Responsibility for animal subject studies initiated by VA investigators, regardless of funding source, cannot be delegated. It remains the responsibility of the VA medical center to ensure that these studies comply with regulations and policies governing the use of animal subjects in experimentation, irrespective of administrative arrangements with affiliated institutions.
- e. A VA medical center that houses animals belonging to an affiliated institution may accept the animal subject protocol review of the affiliated institution provided that the protocol is submitted to, and accepted by the R&D Committee and the SAS of the VA medical center. Such protocols must be maintained on file, subject to review as described in the Federal Regulations, VA Policy, and PHS Policy when applicable.  
NOTE: All animal subject protocols submitted to VA Central Office for VA funding must use the VA Animal Component of Research Protocol (ACORP), see M-3, Part I, Chapter 12, Appendix 12C.
- f. When preparing the USDA Annual Report of Research Facility, it is acceptable to report animals owned by the VA medical center, but housed in an affiliated institution, on the VA medical center report form or the report of the affiliated institution. This practice must be consistent across species. It is recommended that when VA medical center animals are reported by affiliated institutions, a copy of the report of the affiliated institution be retained by the VA medical center. Records of

ownership and research use of such animals must be retrievable at the VA medical center.

## 5. REFERENCES

- a. Manual M-3, Part I, Chapter 12.
- b. Title 7 CFR 2.17, 2.51, and 371.2 (g).
- c. Title 9 CFR Chapter 1 (1-1-92), subchapter A, Animal Welfare.
- d. Title 7 United States Code Sections 2131 through 2157.
- e. OPRR/PHS Policy on Humane Care and Use of Laboratory Animals.

Revised September 1986.

6. RESCISSION: None. This VHA Directive will expire (Date).

7. FOLLOW-UP RESPONSIBILITY: Associate Chief Medical Director for Research and Development (12/4).

S/ by Dennis Smith for  
John T. Farrar, M.D.  
Acting Under Secretary for Health

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# National Aeronautics and Space Administration

## 14 CFR 1232

### CODE OF FEDERAL REGULATIONS

Effective Date August 22, 1989

Responsible Office: UL

Subject: **CARE AND USE OF ANIMALS IN THE CONDUCT OF NASA ACTIVITIES**

#### SECTION

1232.100 Scope.

1232.101 Applicability.

1232.102 Policy.

1232.103 Definitions.

1232.104 Implementation procedures by non-NASA institutions.

1232.105 Implementation procedures by NASA field installations.

1232.106 Management authority and responsibility.

1232.107 Sanctions.

**AUTHORITY:** 42 U.S.C. Sec. 2451; Pub. L. 89-544, as amended; 7 U.S.C. Sec. 2131; 39 U.S.C. Sec. 3001; 9 CFR Subchapter A Parts 1, 2, 3, and 4; and Pub. L. 99-158, Sec. 495.

#### **S 1232.100 Scope.**

This rule establishes the policy, implementation procedures, and management authority and responsibility for the care and use of vertebrate animals (hereinafter referred to as "animal subjects") in the conduct of NASA activities.

#### **S 1232.101 Applicability.**

This rule applies to NASA Headquarters and NASA field installations and will be followed in all activities using animal subjects that are supported by NASA, conducted in NASA facilities, aircraft, or spacecraft, or which involve NASA to any degree. All activities using animal subjects conducted under a contract, grant, cooperative agreement, memorandum of understanding, or joint endeavor agreement entered into by NASA and another Government agency, private entity, non-Federal public entity, or foreign entity are included within the scope of this rule.

#### **S 1232.102 Policy.**

(a) It is NASA policy to require its laboratories and the institutions performing NASA-supported activities using animal subjects to comply with the Animal Welfare Act of 1966 (Pub. L. 89-544), as amended (Pub. L. 91-579, Pub. L. 94-279, and Pub. L. 99-198), 7 U.S.C. Sections 2131 et seq., and 39 U.S.C. Section 3001, and with the regulations promulgated thereunder by the Secretary of Agriculture (9 CFR Subchapter A Parts 1, 2, 3, and 4) pertaining to the care, handling, and treatment of animal subjects held or used for research, testing, teaching, or other activities supported by the Federal government. Investigators shall follow the guidelines described in the National Institutes of Health (NIH) Publication No. 85-23 (Rev. 1985), "Guide for the Care and Use of Laboratory Animals" (the Guide) or subsequent revisions. Attention is called to the U.S. Government "Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training" on pp. 81-83 of the Guide. In order to implement these guidelines and principles, investigators will comply with the revised Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals (hereinafter referred to as PHS Policy) effective November 1, 1986.

(b) This rule authorizes NASA to have the same authority for NASA-supported programs as that delegated to PHS by the PHS Policy, including the functions and responsibilities of the Animal Care and Use Committees (ACUC's).

(c) All research supported by NASA that involves activities using animal subjects shall be conducted under protocols that conform to this rule and that are reviewed and approved as prescribed in this rule.

### **S 1232.103 Definitions.**

The following definitions of terms comply with the PHS Policy and apply to the conduct of all NASA activities related to the care and use of animal subjects.

(a) "Activity" includes research, testing of hardware for animal use, flight experimentation, and any other tasks involving the use of animal subjects.

(b) "Animal" is any live vertebrate animal.

(c) "Animal Care and Use Committee" (ACUC) is the committee established at each institution and NASA field installation involved in research with animal subjects. It is responsible for evaluating the care and use of animal subjects at the facility and for ensuring that the care and use of animal subjects at the facility is in compliance with this rule and PHS Policy.

(d) "Authorized NASA Official" is the Director, Life Sciences Division, NASA Headquarters, or designee, who is the NASA Administrator's representative and is responsible for all NASA activities involving animal subjects. This individual is responsible for implementation of the provisions of this rule and for ensuring that agency programs involving animal subjects comply fully with all applicable laws, regulations, and guidelines.

(e) "Field Installation Director" is the Director of a NASA Field Installation, or designee, who is the institutional official responsible for the care and use of animal subjects in research conducted at that field installation and for ensuring compliance with this rule at that field installation.

(f) "Investigator" is any person who uses or proposes to use live animal subjects in NASA-supported activities, e.g., receives funds, salaries, or support under a grant, award, agreement, contract, or direct employment by NASA, or the use of any NASA facilities, aircraft, or spacecraft for the purpose of carrying out research, tests, or experiments using animal subjects.

(g) "PHS Assurance" is a document prepared by an awardee institution assuring its compliance with PHS Policy.

(h) "Research or Flight Program Manager" is the NASA Headquarters manager of each program in which NASA has a manifest interest.

(i) "Supported" pertains to activities either funded in part or in whole by NASA or an approved activity that is not funded by NASA but that utilizes NASA facilities, including spacecraft and aircraft.

(j) "Veterinarian" is the NASA attending veterinarian, a person who has graduated from a veterinary school accredited by the American Veterinary Medical Association's Council on Education or has a certificate issued by the American Veterinary Medical Association's Education Commission for Foreign Veterinary Graduates, has received training and/or experience in the care and management of the species being attended, and who has direct or delegated authority and responsibility for activities involving animal subjects at the NASA field installation.

### **S 1232.104 Implementation procedures by non-NASA institutions.**

(a) Proposal Information. No animal subjects may be utilized unless a proposal justifying and describing their use is submitted to NASA for approval. The required proposal information is outlined in the PHS Policy (IV.D.1.a.-e.).

(b) Proposal Approval by the Institutional ACUC. Before a proposal for research involving the use of animal subjects will be considered for NASA support, the NASA Headquarters Research or Flight Program Manager must receive a statement that the research has been reviewed in accordance with the PHS Policy (IV.C.) and approved by the appropriate ACUC at the participating institution.

(c) Proposal Approval for Flight Experiments. In addition to the institution's ACUC review, activities involving animal subjects to be flown on NASA spacecraft will be subject to review and approval by the Ames Research Center (ARC) ACUC. The ARC ACUC will submit each evaluation report to the ARC Director who will transmit the report with his/her recommendation to the Authorized NASA Official, NASA Headquarters. Animal activities to be flown onboard NASA manned spacecraft may also be subject to review by the Human Research Policy and Procedures Committee (HRPPC) at the Johnson Space Center (JSC). Animal activities utilizing the facilities of any NASA field installation are also subject to approval of that field installation's ACUC [S1232.105 (d)].

(d) Institutions with PHS Assurance on File. The institution, by an approved or provisionally acceptable Assurance on file at the NIH Office for Protection from Research Risks (OPRR), Department of Health and Human Services (HHS), assures NASA that it will comply with the PHS Policy. The Assurance file number must be included in the research proposal submitted to NASA.

(e) Institutions with No PHS Assurance on File. Proposals from institutions without an approved Assurance on file with the NIH OPRR will first be peer-reviewed for scientific merit. If the proposed research is deemed worthy of support, NASA will arrange for a special Assurance to be negotiated by the Director, Life Sciences Division, NASA Headquarters. The arrangements for a special Assurance review by NIH should be undertaken in consultation with the NASA representative to the Interagency Research Animal Committee (IRAC) and will be handled on a case- by-case basis.

(f) Foreign institutions must comply with the PHS Policy (see Section II of PHS Policy) and this rule before being supported by NASA for any activities involving animal subjects.

### **S 1232.105 Implementation procedures by NASA field installations.**

(a) Proposal Information. The information required for proposals involving the use of animal subjects is identical to that described in S1232.104 (a).

(b) Proposal Approval by the NASA ACUC. Before a proposal for research involving the use of animal subjects will be considered for NASA support, the NASA Headquarters Research or Flight Program Manager must receive a statement that the research has been reviewed in accordance with the PHS Policy (IV.C.) and approved by the ACUC at the appropriate field installation.

(c) Proposal Approval for Flight Experiments. In addition to the Field Installation ACUC review, activities involving animal subjects to be flown on NASA spacecraft will be subject to review and approval by the ARC ACUC. The ARC ACUC will submit each evaluation report to the ARC Director who will transmit the report with his/her recommendation to the Authorized NASA Official, NASA Headquarters. Animal activities to be flown onboard NASA manned spacecraft may also be subject to review by the HRPPC at JSC.



(d) Approval for Use of Field Installation Facilities. The NASA Field Installation ACUC will review and approve or disapprove those parts of proposals that call for the use of their facilities to conduct any activity involving animal subjects (e.g., Kennedy Space Center or ARC Dryden facilities used to support experiments using animal subjects). The ACUC will submit each evaluation report to the Field Installation Director who will transmit the report with his/her recommendation to the Authorized NASA Official, NASA Headquarters.

(e) NASA Animal Care and Use Committees.

(1) The Director of each NASA Field Installation that is involved in animal research activities will establish an ACUC to ensure compliance with the policies and provisions of this rule. The membership of the ACUC shall be in accordance with PHS Policy.

(2) The NASA Field Installation ACUC's will review and approve or disapprove all proposals using animal subjects. In accordance with the PHS Policy (IV.C.), the ACUC will submit each report to the Field Installation Director who will, upon request, transmit the report with his/her recommendation to the Authorized NASA Official, NASA Headquarters.

(3) NASA ACUC's have the authority to approve, disapprove, or require changes to be made in those components of proposals involving the care and use of animal subjects that are submitted by NASA investigators. All decisions shall be based on the response of a majority of a quorum of the members. A minority opinion including abstentions should be recorded; this record should include a justification for the opinion.

(4) The ACUC shall conduct continuing review of proposals at appropriate intervals as determined by the ACUC, but not less than once every 3 years.

(5) Proposals that have been approved by the ACUC may be subject to further appropriate review by the Authorized NASA Official, NASA Headquarters. However, the official may not approve those sections of a proposal related to the care and use of animal subjects if they have not been approved by the ACUC.

(6) Once experimental procedures are approved, no substantial changes can be made unless a formal request with appropriate justification for such a request is submitted to and approved by the appropriate ACUC. If the experiment involves exposure of the flight crew to the animal subjects, the HRPPC at JSC must review and approve the proposed modifications. Copies of ACUC approval of the proposed modifications shall be submitted to the Field Installation Director who will, upon request, transmit the report to the Authorized NASA Official, NASA Headquarters.

(7) Other functions of the field installation ACUC include:

(i) Reviewing at least once every 6 months the field installation's program for humane care and use of animals, using the Guide as a basis for evaluation;

(ii) Inspecting at least once every 6 months all of the field installation's animal facilities (including satellite facilities), using the Guide as a basis for evaluation;

(iii) Preparing reports of the ACUC evaluations conducted as required by S1232.105 (e)(7)(i) and (ii), and submitting the reports to the Field Installation Director. (Note: the reports shall be updated at least once every 6 months upon completion of the required semiannual evaluations and shall be maintained by the field installation and made available to the Authorized NASA Official upon request. The reports must contain a description of the nature and extent of the field installation's adherence to the Guide and this rule and must identify specifically any departures from the provisions of the Guide and this rule, and must state the reasons for each departure. The



reports must distinguish significant deficiencies from minor deficiencies. A significant deficiency is one which, consistent with PHS Policy, and, in the judgment of the ACUC and the Field Installation Director, is or may be a threat to the health or safety of the animals. If program or facility deficiencies are noted, the reports must contain a reasonable and specific plan and schedule for correcting each deficiency.)

(iv) Reviewing concerns involving the care and use of animals at the field installation;

(v) Making recommendations to the Field Installation Director regarding any aspect of the field installation's animal program, facilities, or personnel training.

(f) NASA Assurances. Each NASA field installation involved in activities using animal subjects must assure that its programs and facilities have been evaluated and accredited by the American Association for the Accreditation of Laboratory Animal Care (AAALAC). Written assurance of compliance with the provisions of the PHS Policy and this rule is also required from NASA field installations involved in animal activities before approval of any such activity. This Assurance should follow the sample PHS Assurance format shown on pages 19-26 of the PHS Policy and must be submitted by the Field Installation Director to the Authorized NASA Official. The Assurance is subject to renewal every 5 years.

(g) Recordkeeping Requirements.

(1) Each NASA field installation involved in activities using animal subjects shall maintain:

(i) An Assurance of compliance with PHS Policy and this rule [S1232.105 (f)];

(ii) Minutes of ACUC meetings, including records of attendance, activities of the committee, and committee deliberations;

(iii) Records of applications, proposals, and proposed significant changes in the care and use of animals and whether ACUC approval was given or withheld;

(iv) Records of semiannual ACUC reports and recommendations (including minority views) as forwarded to the Field Installation Director,

(v) Records of AAALAC accreditation; and

(vi) The Field Installation's Animal Users Guide and Animal Care Facility Management Manual. The Field Installation Animal Users Guide and Animal Care Facility Management Manual should be revised at appropriate intervals.

(2) All records shall be maintained for at least 3 years; records that relate directly to applications, proposals, and proposed significant changes in ongoing activities reviewed and approved by the ACUC shall be maintained for the duration of the activity and for an additional 3 years after completion of the activity. All records shall be furnished upon request to the Authorized NASA Official.

(h) Reporting Requirements. For each NASA field installation involved in activities using animal subjects:

(1) Statements of ACUC approval of research proposals, ACUC evaluation reports of flight experiment proposals and of experiment proposals utilizing field installation facilities, and the field installation's Assurance of compliance shall be submitted in the manner prescribed in S1232.104 (c) and S1232.105 (b) (c) (d) and (f).

(2) At least once every 12 months, the ACUC, through the Field Installation Director, shall report in writing to the Authorized NASA Official:

(i) Any change in the field installation's program or facilities that would affect the AAALAC accreditation status;

(ii) Any change in the description of the field installation's program for animal care and use;

(iii) Any changes in the ACUC membership;

(iv) Notice of the dates that the ACUC conducted its semiannual evaluations of the field installation's program and facilities and submitted the evaluations to the Field Installation Director;

(v) A statement that the field installation has no changes to report as specified in S1232.105 (h) (2) (i) (ii) or (iii) of this rule, if there are no changes.

(3) The ACUC, through the Field Installation Director, shall promptly provide the Authorized NASA Official with a full explanation of the circumstances and actions taken with respect to:

(i) Any serious or continuing noncompliance with this rule and PHS Policy;

(ii) Any serious deviation from the provisions of the Guide; or

(iii) Any suspension of an activity by the ACUC.

(4) Reports filed under S1232.105 (h) of this rule shall include any minority views filed by members of the ACUC.

(5) A copy of the U.S. Department of Agriculture (USDA) Annual Report will be furnished to the Authorized NASA Official.

#### **S 1232.106 Management authority and responsibility.**

(a) Authorized NASA Official. The Authorized NASA Official is the NASA Administrator's representative and is responsible for all NASA activities involving animal subjects. This individual is responsible for implementation of the provisions of this rule and for ensuring that agency programs involving animal subjects comply fully with all applicable laws, regulations, and guidelines.

(b) Field Installation Director. The Field Installation Director is responsible for and has the authority to:

(1) sign the field installation's Assurance, making a commitment on behalf of the field installation that the requirements of the PHS Policy and this rule will be met in all field installation activities involving animal subjects;

- (2) create and oversee the functioning of the field installation ACUC;
- (3) decide and administer sanctions in cases of noncompliance with this rule;
- (4) fulfill the reporting requirements assigned to this individual in S1232.105 (h); and
- (5) sign the annual USDA report.

(c) NASA Field Installation(s) ACUC Responsibility. Each NASA Field Installation ACUC is responsible to its Field Installation Director for the activities described in S 1232.104 (c) and S 1232.105 (b) (c) (d) (e) and (h).

(d) Research or Flight Program Manager Responsibility. The Research or Flight Program Manager is responsible for ascertaining the presence of the required PHS Assurance file number for proposals involving animal subjects received from non- NASA institutions, and a statement of ACUC review and approval of all NASA and non-NASA proposals involving animal subjects. No awards for activities involving animal subjects can be made without this documentation [see S1232.104 (b) and (d) and S 1232.105 (b)].

(e) NASA Veterinarian(s) Responsibility. NASA veterinarian(s) have direct or delegated authority and responsibility for activities involving animal subjects at their field installation. Such authority and responsibilities shall include recommending approval or disapproval of procedures involving animal subjects as a member of the ACUC, continual monitoring of these activities, surveillance of the health and condition of animal subjects, and reporting any observed deviations from approved procedures involving animal subjects to the Field Installation Director and the ACUC. In the case of deviation from ACUC- approved practices or procedures, the veterinarian shall have the authority to immediately halt such procedures until they are reviewed and resolved by the ACUC. In cases of a conflict concerning animal usage by an investigator that cannot be resolved between him/her and the veterinarian, the matter may be brought to the attention of the Field Installation ACUC for review and recommendation for action as set forth in this rule. Whereas the performance of the veterinarian's duties can be delegated to other qualified individuals, the ultimate responsibility rests with the veterinarian. This responsibility extends not only to the Animal Care Facility (ACF), but also to other locations where animal subjects are used. Other specific areas of responsibility and authority vested in the veterinarian are:

(1) Entry of personnel into the ACF. The veterinarian has the responsibility to develop access procedures to the ACF and submit them to the ACUC for approval.

(2) Personnel Training. The veterinarian will participate in the training of personnel in the handling of animal subjects and in specimen sampling procedures.

(3) Animal Training. The veterinarian will monitor all schedules and procedures involving the training and acclimation of animal subjects.

(4) Surgery and Surgical Procedures. The veterinarian will monitor all surgical procedures and verify that the principles of the Guide with regard to aseptic surgery are employed. Post- surgical recovery procedures are included. If necessary, training will be provided by the veterinarian to bring procedures conducted by investigators to the level of these standards.

(5) Veterinary Medical and Engineering Procedures. The veterinarian will monitor all veterinary medical and engineering procedures performed on animal subjects and verify their appropriateness. The veterinarian will actively participate in identifying and/or establishing the design requirements and adequacy of animal facilities for ground and spaceflight-related activities.



(f) NASA Representative to the Interagency Research Animal Committee (IRAC). The NASA representative to the IRAC will obtain information of all cases in which an institution's Assurance has been revoked by the PHS. The NASA IRAC representative will notify NASA ACUC's, Field Installation Directors, the Authorized NASA Official, and all Headquarters Research and Flight Program Managers so that they can determine which NASA awards involving the use of animal subjects are affected and can take appropriate sanctions.

#### **S 1232.107 Sanctions.**

(a) Non-NASA Institutions. Principal investigators not employed by NASA whose activities are supported by NASA but whose activities using animal subjects are restricted to non-NASA facilities shall be subject to the control of their institution's ACUC and responsible institutional official. Notification of noncompliance with this rule shall be made either as described in S 1232.106 (f) or by the non-NASA institution to the Director of the NASA Field Installation through which the activity has been supported and to the Authorized NASA Official. Any continued noncompliance may be cause for termination of funding or support.

#### **(b) NASA Field Installations.**

(1) Inappropriate procedures on animal subjects by NASA principal investigators shall be halted by the NASA Field Installation Veterinarian or line management and brought to the attention of the ACUC if the issue cannot be immediately resolved. The ACUC will review the activity and report any noncompliance with this rule to the Field Installation Director. Principal investigators not employed by NASA, whose activities using animal subjects are performed in NASA facilities, aircraft, or spacecraft, are subject to similar action. Such noncompliance will be cause for sanctions. The principal investigator can contest, in writing, these decisions to the ACUC.

(2) The ACUC as the agent of the Field Installation Director may suspend an activity that it previously approved if it determines that the activity is not being conducted in accordance with applicable provisions of the Animal Welfare Act, the Guide, PHS Policy requirements, or this rule.

(3) Any suspension or termination of approval will include a statement of the reasons for the action and will be promptly reported to the principal investigator and the appropriate Field Installation Director. In the case of investigators from non-NASA institutions, notification should be sent to the investigator, the appropriate institution, and the Director of the Field Installation through which the activity has been supported. If the ACUC suspends an activity involving animal subjects, the Field Installation Director in consultation with the ACUC shall review the reasons for suspension, take appropriate corrective action, and report that action with a full explanation to the Authorized NASA Official, NASA Headquarters. If an ACUC recommends disapproval, suspension, termination, or conditional approval of an activity, the principal investigator will be given the opportunity to ask for reconsideration of the decision in person and/or in writing to the appropriate NASA ACUC.

(4) If, after notification of the Field Installation Director and an opportunity for correction, such deficiencies or deviations remain uncorrected, the ACUC will notify (in writing) the Authorized NASA Official, NASA Headquarters, who is then responsible for all corrective action to be taken.

/s/Richard H. Truly  
Administrator  
National Aeronautics and Space Administration



# NASA Policy Directive

## **Directive: NPD 8910.1**

Effective Date: March 23, 1998

Expiration Date: March 23, 2003

Responsible Office: UL / Life Sciences Division

Subject: **Care and Use of Animals**

## **1. POLICY**

a. NASA will conduct activities involving vertebrate animals, recognizing its responsibility for the stewardship of the animals and to the scientific community and society and adhering to the ethical principles of respect for life, societal benefit, and non-maleficence.

b. All activities to which this NPD applies will comply with the "Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals"(PHS Policy) and the guidelines in the National Research Council's "Guide for the Care and Use of Laboratory Animals" (the Guide).

c. All NASA Centers (including Component Facilities) conducting activities, regardless of funding source, involving animals will, at all times, be covered by a current Animal Welfare Assurance (Assurance) approved by the Office for Protection from Research Risks (OPRR), National Institutes of Health.

d. All NASA Centers (including Component Facilities) conducting activities involving animals will actively seek to receive and maintain accreditation by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC International).

## **2. APPLICABILITY**

This NPD applies to NASA Headquarters and NASA Centers, including Component Facilities, and to all activities involving animals funded by or sponsored by NASA, or conducted in or on NASA facilities, aircraft, or spacecraft. Such activities include those conducted under a cooperative agreement or grant, reimbursable agreement, or other arrangement or agreement, entered into by NASA and another Government agency, private entity, non-Federal public entity, or foreign entity.

## **3. AUTHORITY**

a. 42 U.S.C. Sec. 2473(c)(1), Sec. 203(c)(1) of the National Aeronautics and Space Act of 1958, as amended.

b. 7 U.S.C. Sec. 2131 et seq., the Animal Welfare Act of 1966, as amended.

## **4. REFERENCES**

a. 14 CFR Part 1232, *Care and Use of Animals in the conduct of NASA Activities*.

b. U.S. Department of Health and Human Services, *Public Health Service Policy on Humane Care and Use of Laboratory Animals* (1986).

- c. National Research Council, *Guide for the Care and Use of Laboratory Animals* (1996).
- d. United States Interagency Research Animal Committee, *U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training* (1985).
- e. Council for International Organizations of Medical Sciences, *International Guiding Principles for Biomedical Research Involving Animals* (1985).
- f. 9 CFR Subchapter A, Parts 1,2,3, and 4, U.S. Department of Agriculture (USDA), Animal Welfare.

## 5. RESPONSIBILITY

- a. The Associate Administrator for the Office of Life and Microgravity Sciences and Applications (AA for Code U) has overall responsibility for this NPD, including the designation of the authorized NASA official.
- b. The Director of the Life Sciences Division (Code UL) will be the authorized NASA official responsible for the following:
  - (1) Implementing the provisions of this NPD and ensuring that all Agency programs and activities involving animals comply fully with all applicable laws, regulations, and guidelines.
  - (2) Representing NASA on, or designating a representative for, the Federal Interagency Research Animal Committee (IRAC).
  - (3) Establishing and maintaining mechanisms for obtaining timely information from OPRR of all cases in which the Assurance of an institution involved in NASA research has been withdrawn by the PHS; and notifying NASA's Institutional Animal Care and Use Committees (IACUC), Center Directors, and Research and Flight Program Managers of such revocations so that they can determine if NASA awards involving the use of animals are affected and take appropriate actions. The authorized NASA official may designate a representative for these functions.
  - (4) Reviewing all sanctions imposed by Center Directors or IACUC's to determine if further sanctions are warranted or, at his or her discretion, initiating investigations of alleged noncompliance with this NPD and imposing sanctions when warranted.
  - (5) Appointing the NASA Chief Veterinarian, who will be a NASA civil service employee.
- c. Center Directors are responsible for the following:
  - (1) Signing the Center's Assurance, making a commitment on behalf of the Center that the requirements of this NPD will be met. Center Directors may delegate authority for the day-to-day management of their Centers' Animal Care and Use Program but they retain the ultimate responsibility for ensuring compliance with this NPD, the Animal Welfare Act, PHS policy, and the Guide at their Centers.
  - (2) Establishing and supervising the functioning of their Centers' IACUC. This responsibility may be accomplished through the use of another Center's IACUC via a formal inter-Center agreement.
  - (3) Signing and submitting to OPRR the Animal Welfare Assurance, committing the Center to the requirements of the PHS policy and this NPD in all Center activities involving animal

subjects and providing copies of the approved Assurance, OPRR letter of approval, and any OPRR correspondence to the authorized NASA official.

(4) Signing the application for AAALAC International Accreditation and the annual AAALAC International reports, and providing copies of the AAALAC International Accreditation letter, the annual reports, and any correspondence from AAALAC International to the authorized NASA official.

(5) Signing the annual report to USDA and providing copies of the report and any comments from USDA to the authorized NASA official.

(6) Deciding and administering sanctions in cases of noncompliance with this NPD in accordance with the Animal Welfare Act, PHS policy, and applicable NASA regulations, and notifying appropriate funding officials and the authorized NASA official.

(7) Providing the authorized NASA official with copies of all IACUC minutes and reports.

d. The NASA IACUC's are responsible for approving any animal use conducted at their Centers.

e. The NASA Ames Research Center (ARC) IACUC, in addition to approving any animal use conducted at ARC, is responsible for reviewing and approving all NASA-supported flight activities in the United States involving animals, regardless of launch site or site of performance (includes both aircraft and spacecraft vehicles). This responsibility may be delegated to another Agency IACUC with the approval of the authorized NASA official. The ARC IACUC will also review all NASA-supported flight activities involving animals which are conducted in other countries; however, the primary responsibility for those activities rests with the host country.

f. The NASA Chief Veterinarian is responsible for the following:

(1) Coordinating veterinary and animal care activities on an Agencywide basis. In accomplishing this responsibility, the NASA Chief Veterinarian is specifically authorized to suspend any animal activity believed to be noncompliant with applicable laws, regulations, this policy, and approved protocols. Following suspension of any activity, the Chief Veterinarian will initiate action, including IACUC re-review, to resolve the situation.

(2) Guiding, as Chairperson, the activities of the Intercenter Animal Care and Use Coordination Team (IACUCT), composed of Center veterinarians (serving, on a rotating basis, as Executive Secretary); Chairs of each Center's IACUC; other representatives of each Center as appointed by Center Directors; and a public affairs specialist, a legal advisor, and others, as appointed by the authorized NASA official.

(3) Advising the authorized NASA official on any aspect of the Agency's Animal Care and Use Program.

(4) Representing NASA in the external laboratory animal science community and associations such as the American Association for Laboratory Animal Science and the American College of Laboratory Animal Medicine.

(5) Maintaining coordination with the International Council for Laboratory Animal Science (ICLAS);

(6) Participating in development of requirements for all animal facilities and equipment for flight as related to animal care and use.

(7) Developing and implementing a program to foster and encourage the use of alternate methods of research that reduce the numbers of animals used, refine the procedures used to minimize or eliminate animal pain or distress, or encourage the use of procedures that do not require the use of animals. As part of this effort, the NASA Chief Veterinarian will establish and maintain liaison with organizations working in this field and will develop and maintain mechanisms for dissemination of information regarding new methods and protocols to potentially interested parties.

(8) Developing and implementing for non-NASA investigators an education program intended to inform them regarding the requirements and constraints for flight animal research activities inflight.

(9) Informing foreign entities and individuals about the technical requirements in accordance with U.S. laws, regulations, guidelines, standards, and this NPD. This will include information regarding the requirements and constraints for flight animal research activities, as well as sources for electronic and hard copy access to animal care and use information.

## **6. DELEGATION OF AUTHORITY**

None.

## **7. MEASUREMENTS**

Adherence to this NPD will be measured through strict implementation of requirements outlined herein and detailed in NASA NPG 8910. In general terms, for all NASA-sponsored research involving animals, the requirements will include accreditation and certifications, review and approval by the appropriate IACUC's, and specified monitoring.

## **8. CANCELLATION**

None.

/s/ Daniel S. Goldin  
Administrator  
National Aeronautics and Space Administration



# NASA Principles for the Ethical Care and Use of Animals

A strong allegiance to the principles of bioethics is vital to any discussion of responsible research practices. As reflected in the considerations of the National Commission for the Protection of Human Subjects, "scientific research has produced substantial social benefits ... [and] some troubling ethical questions" (The Belmont Report, 1979). The Belmont Report identified the key fundamental principles underlying the ethical evaluation of research involving human subjects. Similarly, the principles governing the ethical evaluation of the use of animals in research must be made equally explicit.

It is generally agreed that vertebrate animals warrant moral concern. The following principles are offered to guide careful and considered discussion of the ethical challenges that arise in the course of animal research, a process that must balance risks, burdens, and benefits. NASA will abide by these principles as well as all applicable laws and policies that govern the ethical use of animals (see list at end). It is recognized that awareness of these principles will not prevent conflicts. Rather, these principles are meant to provide a framework within which challenges can be rationally addressed.

## Basic Principles

The use of animals in research involves responsibility, not only for the stewardship of the animals but to the scientific community and society as well. Stewardship is a universal responsibility that goes beyond the immediate research needs to include acquisition, care and disposition of the animals, while responsibility to the scientific community and society requires an appropriate understanding of and sensitivity to scientific needs and community attitudes toward the use of animals.

Among the basic principles generally accepted in our culture, three are particularly relevant to the ethics of research using animals: respect for life, societal benefit, and non-maleficence.

### 1. Respect for Life

Living creatures deserve respect. This principle requires that animals used in research should be of an appropriate species and health status and that the research should involve the minimum number of animals required to obtain valid scientific results. It also recognizes that the use of different species may raise various ethical concerns. Selection of appropriate species should consider cognitive capacity and other morally relevant factors. Additionally, methods such as mathematical models, computer simulation, and in vitro systems should be considered and used whenever possible.

### 2. Societal Benefit

The advancement of biological knowledge and the improvements in the protection of the health and well being of both humans and other animals provide strong justification for biomedical and behavioral research. This principle entails that in cases where animals are used, the assessment of the overall ethical value of such use should include consideration of the full range of potential societal goods, the populations affected, and the burdens that are expected to be borne by the subjects of the research.

### 3. Non-maleficence

Vertebrate animals are sentient. This principle entails that the minimization of distress, pain, and suffering is a moral imperative. Unless the contrary is established, investigators should consider that procedures that cause pain or distress in humans may cause pain or distress in other sentient animals.

# Public Health Service Policy on Humane Care and Use of Laboratory Animals

Revised September, 1986

Reprinted March, 1996

NATIONAL INSTITUTES OF HEALTH

OFFICE OF THE DIRECTOR

## PREFACE

The full-text of this policy may be found at <http://www.nih.gov:80/grants/oprr/phspol.htm>

This 1996 reprint of the Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals is substantively identical to the original Policy promulgated in 1986 to implement the Health Research Extension Act of 1985 (Public Law 99-158). Citations and addresses are updated and some language is clarified to eliminate common areas of confusion. The U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training appear in a more prominent location to emphasize their importance.

The Office for Protection from Research Risks (OPRR) at the National Institutes of Health, which has responsibility for the general administration and coordination of the Policy on behalf of the PHS, provides specific guidance, instruction, and materials to institutions that must comply with the Policy. For copies of supplemental materials, please contact OPRR at the National Institutes of Health, 6100 Executive Boulevard, MSC 7507, Suite 3B01, Rockville, Maryland 20892-7507. To obtain faxed copies of supplemental materials, please call the OPRR FAXCALL Service at 301-594-0464.

## ABSTRACT OF PHS POLICY

The Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals sets forth the requirements that are applicable to all research, research training, biological testing, and related activities involving animals that are supported or conducted by agencies of the PHS. The Office for Protection from Research Risks (OPRR) at the National Institutes of Health is responsible for the general administration and coordination of the Policy.

The Policy is mandated by the Health Research Extension Act of 1985 (Public law 99-158), and implements the U.S. Government Principles for the Utilization and Care of Vertebrate Animals used in Testing, Research, and Training. Included in the Policy are institutional responsibilities for Animal Welfare Assurances, Institutional Animal Care and Use Committees (IACUCs), review of projects, programmatic evaluations, facility inspections, record keeping and reporting. Specific criteria for IACUC review of projects, and frequency and methods of review are described. The information required by the PHS in applications or proposals when animals are to be involved, and PHS responsibilities for implementing the Policy, are also included.

5/09/96

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### **U.S. GOVERNMENT PRINCIPLES FOR THE UTILIZATION AND CARE OF VERTEBRATE ANIMALS USED IN TESTING, RESEARCH, AND TRAINING**

The development of knowledge necessary for the improvement of the health and well-being of humans as well as other animals requires in vivo experimentation with a wide variety of animal species. Whenever U.S. Government agencies develop requirements for testing, research, or training procedures involving the use of vertebrate animals, the following principles shall be considered; and whenever these agencies actually perform or sponsor such procedures, the responsible Institutional Official shall ensure that these principles are adhered to:

I. The transportation, care, and use of animals should be in accordance with the Animal Welfare Act (7 U.S.C. 2131 et. seq.) and other applicable Federal laws, guidelines, and policies.\*

II. Procedures involving animals should be designed and performed with due consideration of their relevance to human or animal health, the advancement of knowledge, or the good of society.

III. The animals selected for a procedure should be of an appropriate species and quality and the minimum number required to obtain valid results. Methods such as mathematical models, computer simulation, and in vitro biological systems should be considered.

IV. Proper use of animals, including the avoidance or minimization of discomfort, distress, and pain when consistent with sound scientific practices, is imperative. Unless the contrary is established, investigators should consider that procedures that cause pain or distress in human beings may cause pain or distress in other animals.

V. Procedures with animals that may cause more than momentary or slight pain or distress should be performed with appropriate sedation, analgesia, or anesthesia. Surgical or other painful procedures should not be performed on unanesthetized animals paralyzed by chemical agents.

VI. Animals that would otherwise suffer severe or chronic pain or distress that cannot be relieved should be painlessly killed at the end of the procedure or, if appropriate, during the procedure.

VII. The living conditions of animals should be appropriate for their species and contribute to their health and comfort. Normally, the housing, feeding, and care of all animals used for biomedical purposes must be directed by a veterinarian or other scientist trained and experienced in the proper care, handling, and use of the species being maintained or studied. In any case, veterinary care shall be provided as indicated.

VIII. Investigators and other personnel shall be appropriately qualified and experienced for conducting procedures on living animals. Adequate arrangements shall be made for their in-service training, including the proper and humane care and use of laboratory animals.



IX. Where exceptions are required in relation to the provisions of these Principles, the decisions should not rest with the investigators directly concerned but should be made, with due regard to Principle II, by an appropriate review group such as an institutional animal care and use committee. Such exceptions should not be made solely for the purposes of teaching or demonstration.

\*For guidance throughout these Principles, the reader is referred to the Guide for the Care and Use of Laboratory Animals prepared by the Institute of Laboratory Animal Resources, National Academy of Sciences

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## **PUBLIC HEALTH SERVICE POLICY ON HUMANE CARE AND USE OF LABORATORY ANIMALS**

### **I. INTRODUCTION**

It is the Policy of the Public Health Service (PHS) to require institutions to establish and maintain proper measures to ensure the appropriate care and use of all animals involved in research, research training, and biological testing activities (hereinafter referred to as activities) conducted or supported by the PHS. The PHS endorses the "U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training" developed by the Interagency Research Animal Committee. This Policy is intended to implement and supplement those Principles.

### **II. APPLICABILITY**

This Policy is applicable to all PHS-conducted or supported activities involving animals, whether the activities are performed at a PHS agency, an awardee institution, or any other institution and conducted in the United States, the Commonwealth of Puerto Rico, or any territory or possession of the United States. Institutions in foreign countries receiving PHS support for activities involving animals shall comply with this Policy, or provide evidence to the PHS that acceptable standards for the humane care and use of the animals in PHS-conducted or supported activities will be met. No PHS support for an activity involving animals will be provided to an individual unless that individual is affiliated with or sponsored by an institution which can and does assume responsibility for compliance with this Policy, unless the individual makes other arrangements with the PHS. This Policy does not affect applicable state or local laws or regulations which impose more stringent standards for the care and use of laboratory animals. All institutions are required to comply, as applicable, with the Animal Welfare Act, and other Federal statutes and regulations relating to animals.

### **III. DEFINITIONS**

#### *A. Animal*

Any live, vertebrate animal used or intended for use in research, research training, experimentation, or biological testing or for related purposes.

#### *B. Animal Facility*

Any and all buildings, rooms, areas, enclosures, or vehicles, including satellite facilities, used for animal confinement, transport, maintenance, breeding, or experiments inclusive of surgical manipulation. A satellite facility is any containment outside of a core facility or centrally designated or managed area in which animals are housed for more than 24 hours.

#### *C. Animal Welfare Act*

Public Law 89-544, 1966, as amended, (P.L. 91-579, P.L. 94-279 and P.L. 99-198) 7 U.S.C. 2131 et. seq. Implementing regulations are published in the Code of Federal Regulations (CFR), Title 9, Chapter 1, Subchapter A, Parts 1, 2, and 3, and are administered by the U.S. Department of Agriculture.

#### *D. Animal Welfare Assurance or Assurance*



The documentation from an institution assuring institutional compliance with this Policy.

*E. Guide*

Guide for the Care and Use of Laboratory Animals, HHS, NIH Pub. No. 86-23, 1985 edition or succeeding revised editions.

*F. Institution*

Any public or private organization, business, or agency (including components of Federal, state, and local governments).

*G. Institutional Official*

An individual who signs, and has the authority to sign the institution's Assurance, making a commitment on behalf of the institution that the requirements of this Policy will be met.

*H. Public Health Service*

The Public Health Service or PHS currently includes the Agency for Health Care Policy Research, the Centers for Disease Control and Prevention, the Food and Drug Administration, the Health Resources and Services Administration, the Indian Health Service, the National Institutes of Health, and the Substance Abuse and Mental Health Services Administration.

*I. Quorum*

A majority of the members of the Institutional Animal Care and Use Committee (IACUC).

## **IV. IMPLEMENTATION BY INSTITUTIONS**

### **A. Animal Welfare Assurance**

No activity involving animals may be conducted or supported by the PHS until the institution conducting the activity has provided a written Assurance acceptable to the PHS, setting forth compliance with this Policy. Assurances shall be submitted to the Office for Protection from Research Risks (OPRR), Office of the Director, National Institutes of Health.<sup>1</sup> The Assurance shall be typed on the institution's letterhead and signed by the Institutional Official. OPRR will provide the institution with necessary instructions and an example of an acceptable Assurance. All Assurances submitted to the PHS in accordance with this Policy will be evaluated by OPRR to determine the adequacy of the institution's proposed program for the care and use of animals in PHS-conducted or supported activities. On the basis of this evaluation OPRR may approve or disapprove the Assurance, or negotiate an approvable Assurance with the institution. Approval of an Assurance will be for a specified period of time (no longer than five years) after which time the institution must submit a new Assurance to OPRR. OPRR may limit the period during which any particular approved Assurance shall remain effective or otherwise condition, restrict, or withdraw approval. Without an applicable PHS-approved Assurance no PHS-conducted or supported activity involving animals at the institution will be permitted to continue.

#### **1. Institutional Program for Animal Care and Use**

The Assurance shall fully describe the institution's program for the care and use of animals in PHS-conducted or supported activities. The PHS requires institutions to use the Guide for the Care and Use of Laboratory Animals (Guide) as a basis for developing and implementing an institutional program for activities involving animals.<sup>2</sup> The program description must include the following:

- a. a list of every branch and major component of the institution, as well as a list of every branch and major component of any other institution, which is to be included under the Assurance;
- b. the lines of authority and responsibility for administering the program and ensuring compliance with this Policy;
- c. the qualifications, authority, and responsibility of the veterinarian(s) who will participate in the program and the percent of time each will contribute to the program;

- d. the membership list of the Institutional Animal Care and Use Committee(s) (IACUC) established in accordance with the requirements set forth in IV.A.3. of this Policy;<sup>3</sup>
- e. the procedures which the IACUC will follow to fulfill the requirements set forth in this Policy;
- f. the health program for personnel who work in laboratory animal facilities or have frequent contact with animals;
- g. a synopsis of training or instruction in the humane practice of animal care and use, as well as training or instruction in research or testing methods that minimize the number of animals required to obtain valid results and minimize animal distress, offered to scientists, animal technicians, and other personnel involved in animal care, treatment, or use;
- h. the gross square footage of each animal facility (including satellite facilities), the species housed therein and the average daily inventory, by species, of animals in each facility; and
- i. any other pertinent information requested by OPRR.

## **2. Institutional Status**

Each institution must assure that its program and facilities are in one of the following categories:

Category 1 - Accredited by the American Association for Accreditation of Laboratory Animal Care (AAALAC). All of the institution's programs and facilities (including satellite facilities) for activities involving animals have been evaluated and accredited by AAALAC, or another accrediting body recognized by PHS.<sup>4</sup> All of the institution's programs and facilities (including satellite facilities) for activities involving animals have also been evaluated by the IACUC and will be reevaluated by the IACUC at least once every six months, in accordance with IV.B.1. and 2. of this Policy, and reports prepared in accordance with IV.B.3. of this Policy.

Category 2 - Evaluated by the Institution. All of the institution's programs and facilities (including satellite facilities) for activities involving animals have been evaluated by the IACUC and will be reevaluated by the IACUC at least once every six months, in accordance with IV.B.1. and 2. of this Policy, and reports prepared in accordance with IV.B.3. of this Policy. The most recent semi-annual report of the IACUC evaluation shall be submitted to OPRR with the Assurance.

## **3. Institutional Animal Care and Use Committee (IACUC)**

a. The Chief Executive Officer shall appoint an Institutional Animal Care and Use Committee (IACUC), qualified through the experience and expertise of its members to oversee the institution's animal program, facilities, and procedures.<sup>5</sup>

b. The Assurance must include the names, position titles, and credentials of the IACUC chairperson and the members. The committee shall consist of not less than five members, and shall include at least:

- (1) one Doctor of Veterinary Medicine, with training or experience in laboratory animal science and medicine, who has direct or delegated program authority and responsibility for activities involving animals at the institution (see IV.A.1.c.);
- (2) one practicing scientist experienced in research involving animals;
- (3) one member whose primary concerns are in a nonscientific area (for example, ethicist, lawyer, member of the clergy); and
- (4) one individual who is not affiliated with the institution in any way other than as a member of the IACUC, and is not a member of the immediate family of a person who is affiliated with the institution.

c. An individual who meets the requirements of more than one of the categories detailed in IV.A.3.b.(1)-(4) of this policy may fulfill more than one requirement. However, no committee may consist of less than five members.

## **B. Functions of the Institutional Animal Care and Use Committee**

As an agent of the institution, the IACUC shall with respect to PHS - conducted or supported activities:

1. review at least once every six months the institution's program for humane care and use of animals, using the Guide as a basis for evaluation;<sup>6</sup>
2. inspect at least once every six months all of the institution's animal facilities (including satellite facilities) using the Guide as a basis for evaluation;<sup>7</sup>
3. prepare reports of the IACUC evaluations conducted as required by IV.B.1. and 2. of this Policy, and submit the reports to the Institutional Official. (NOTE: the reports shall be updated at least once every six months upon completion of the required semiannual evaluations and shall be maintained by the institution and made available to OPRR upon request. The reports must contain a description of the nature and extent of the institution's adherence to the Guide and this Policy and must identify specifically any departures from the provisions of the Guide and this Policy, and must state the reasons for each departure. The reports must distinguish significant deficiencies from minor deficiencies. A significant deficiency is one which, consistent with this Policy, and, in the judgment of the IACUC and the Institutional Official, is or may be a threat to the health or safety of the animals. If program or facility deficiencies are noted, the reports must contain a reasonable and specific plan and schedule for correcting each deficiency. If some or all of the institution's facilities are accredited by AAALAC or another accrediting body recognized by PHS, the report should identify those facilities as such.);
4. review concerns involving the care and use of animals at the institution;
5. make recommendations to the Institutional Official regarding any aspect of the institution's animal program, facilities, or personnel training;
6. review and approve, require modifications in (to secure approval) or withhold approval of those components of PHS-conducted or supported activities related to the care and use of animals as specified in IV.C. of this Policy;
7. review and approve, require modifications in (to secure approval), or withhold approval of proposed significant changes regarding the use of animals in ongoing activities; and
8. be authorized to suspend an activity involving animals in accordance with the specifications set forth in IV.C.6 of this Policy.

## **C. Review of PHS-Conducted or Supported Research Projects**

1. In order to approve proposed research projects or proposed significant changes in ongoing research projects, the IACUC shall conduct a review of those components related to the care and use of animals and determine that the proposed research projects are in accordance with this Policy. In making this determination, the IACUC shall confirm that the research project will be conducted in accordance with the Animal Welfare Act insofar as it applies to the research project, and that the research



project is consistent with the Guide unless acceptable justification for a departure is presented.<sup>8</sup> Further, the IACUC shall determine that the research project conforms with the institution's Assurance and meets the following requirements:

- a. Procedures with animals will avoid or minimize discomfort, distress, and pain to the animals, consistent with sound research design.
- b. Procedures that may cause more than momentary or slight pain or distress to the animals will be performed with appropriate sedation, analgesia, or anesthesia, unless the procedure is justified for scientific reasons in writing by the investigator.
- c. Animals that would otherwise experience severe or chronic pain or distress that cannot be relieved will be painlessly killed at the end of the procedure or, if appropriate, during the procedure.
- d. The living conditions of animals will be appropriate for their species and contribute to their health and comfort. The housing, feeding, and nonmedical care of the animals will be directed by a veterinarian or other scientist trained and experienced in the proper care, handling, and use of the species being maintained or studied.
- e. Medical care for animals will be available and provided as necessary by a qualified veterinarian.
- f. Personnel conducting procedures on the species being maintained or studied will be appropriately qualified and trained in those procedures.
- g. Methods of euthanasia used will be consistent with the recommendations of the American Veterinary Medical Association (AVMA) Panel on Euthanasia, unless a deviation is justified for scientific reasons in writing by the investigator.<sup>9</sup>

2. Prior to the review, each IACUC member shall be provided with a list of proposed research projects to be reviewed. Written descriptions of research projects that involve the care and use of animals shall be available to all IACUC members, and any member of the IACUC may obtain, upon request, full committee review of those research projects. If full committee review is not requested, at least one member of the IACUC, designated by the chairperson and qualified to conduct the review, shall review those research projects and have the authority to approve, require modifications in (to secure approval) or request full committee review of those research projects. If full committee review is requested, approval of those research projects may be granted only after review at a convened meeting of a quorum of the IACUC and with the approval vote of a majority of the quorum present. No member may participate in the IACUC review or approval of a research project in which the member has a conflicting interest (e.g., is personally involved in the project) except to provide information requested by the IACUC; nor may a member who has a conflicting interest contribute to the constitution of a quorum.

3. The IACUC may invite consultants to assist in the review of complex issues. Consultants may not approve or withhold approval of an activity or vote with the IACUC unless they are also members of the IACUC.

4. The IACUC shall notify investigators and the institution in writing of its decision to approve or withhold approval of those activities related to the care and use of animals, or of modifications required to secure IACUC approval. If the IACUC decides to withhold approval of an activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing.

5. The IACUC shall conduct continuing review of each previously approved, ongoing activity covered by this Policy at appropriate intervals as determined by the IACUC, including a complete review in accordance with IV.C.1.-4. at least once every three years.

6. The IACUC may suspend an activity that it previously approved if it determines that the activity is not being conducted in accordance with applicable provisions of the Animal



Welfare Act, the Guide, the institution's Assurance, or IV.C.1.a.-g. of this Policy. <sup>10</sup> The IACUC may suspend an activity only after review of the matter at a convened meeting of a quorum of the IACUC and with the suspension vote of a majority of the quorum present.

7. If the IACUC suspends an activity involving animals, the Institutional Official in consultation with the IACUC shall review the reasons for suspension, take appropriate corrective action, and report that action with a full explanation to OPRR.

8. Applications and proposals that have been approved by the IACUC may be subject to further appropriate review and approval by officials of the institution. However, those officials may not approve an activity involving the care and use of animals if it has not been approved by the IACUC.

## **D. Information Required in Applications-Proposals for Awards Submitted to PHS**

### **1. All Institutions**

Applications and proposals (competing and non-competing) for awards submitted to PHS that involve the care and use of animals shall contain the following information:

- a. identification of the species and approximate number of animals to be used;
- b. rationale for involving animals, and for the appropriateness of the species and numbers to be used;
- c. a complete description of the proposed use of the animals;
- d. a description of procedures designed to assure that discomfort and injury to animals will be limited to that which is unavoidable in the conduct of scientifically valuable research, and that analgesic, anesthetic, and tranquilizing drugs will be used where indicated and appropriate to minimize discomfort and pain to animals; and
- e. a description of any euthanasia method to be used.

Non-competing applications and contract proposals for other than full and open competitions need not repeat the information required by IV.D.1.a.-e. if the information was complete in the last competing application or proposal and there are no significant changes to that information. However, the application or proposal must contain a statement to that effect. If there are significant changes in the information, then the application or proposal must specifically identify them and state the reasons for the changes.

### **2. Institutions That Have an Approved Assurance**

Applications or proposals (competing and non-competing) covered by this Policy from institutions which have an approved Assurance on file with OPRR shall include verification of approval (including the date of the most recent approval) by the IACUC of those components related to the care and use of animals. For competing applications or proposals only, such verification may be filed at a time not to exceed 60 days after the receipt deadline date. If verification of IACUC approval is submitted subsequent to the submission of the application or proposal, the verification shall state the modifications, if any, required by the IACUC. The verification shall be signed by an individual authorized by the institution, but need not be signed by the Institutional Official.

### **3. Institutions That Do Not Have an Approved Assurance**

For applications and proposals covered by this Policy from institutions that do not have an approved Assurance on file with OPRR, the signature of the official signing for the applicant organization shall constitute a declaration that the institution will submit an Assurance when requested by OPRR. Upon such request, the institution shall prepare the Assurance as instructed by OPRR and in accordance with IV.A. of this Policy. The authorized IACUC shall review those components of the application or proposal as required by IV.C. of this Policy. Upon IACUC approval of those components of the application or proposal the institution shall submit the Assurance to OPRR.

## **E. Recordkeeping Requirements**

1. The awardee institution shall maintain:
  - a. a copy of the Assurance which has been approved by the PHS;
  - b. minutes of IACUC meetings, including records of attendance, activities of the committee, and committee deliberations;
  - c. records of applications, proposals, and proposed significant changes in the care and use of animals and whether IACUC approval was given or withheld;
  - d. records of semiannual IACUC reports and recommendations (including minority views) as forwarded to the Institutional Official; and
  - e. records of accrediting body determinations.
2. All records shall be maintained for at least three years; records that relate directly to applications, proposals, and proposed significant changes in ongoing activities reviewed and approved by the IACUC shall be maintained for the duration of the activity and for an additional three years after completion of the activity. All records shall be accessible for inspection and copying by authorized OPRR or other PHS representatives at reasonable times and in a reasonable manner.

## **F. Reporting Requirements**

1. At least once every 12 months, the IACUC, through the Institutional Official, shall report in writing to OPRR:
  - a. any change in the institution's program or facilities which would place the institution in a different category than specified in its Assurance (see IV.A.2. of this Policy);
  - b. any change in the description of the institution's program for animal care and use as required by IV.A.1.a.-i. of this Policy;
  - c. any changes in the IACUC membership; and
  - d. notice of the dates that the IACUC conducted its semiannual evaluations of the institution's program and facilities and submitted the evaluations to the Institutional Official.
2. At least once every 12 months, the IACUC, at an institution which has no changes to report as specified in IV.F.1.a.-c. of this Policy, shall submit a letter, through the Institutional Official, to OPRR stating that there are no changes and informing OPRR of the dates of the required IACUC evaluations and submissions to the Institutional Official.
3. The IACUC, through the Institutional Official, shall promptly provide OPRR with a full explanation of the circumstances and actions taken with respect to:
  - a. any serious or continuing noncompliance with this Policy;
  - b. any serious deviation from the provisions of the Guide; <sup>11</sup> or

c. any suspension of an activity by the IACUC.

4. Reports filed under IV.F. of this Policy shall include any minority views filed by members of the IACUC.

## **V. IMPLEMENTATION BY PHS**

### **A. Responsibilities of the Office for Protection from Research Risks (OPRR)**

OPRR is responsible for the general administration and coordination of this Policy and will:

1. request and negotiate, approve or disapprove, and, as necessary, restrict or withdraw approval of Assurances;
2. distribute to Scientific Review Administrators of initial review and technical evaluation groups, and to PHS awarding units, lists of institutions that have an approved Assurance;
3. advise awarding units and awardee institutions concerning the implementation of this Policy;
4. evaluate allegations of noncompliance with this Policy;
5. have the authority to review and approve or disapprove waivers to this Policy (see V.D. of this Policy); and
6. conduct site visits to selected institutions.

### **B. Responsibilities of PHS Awarding Units**

PHS awarding units may not make an award for an activity involving animals unless the prospective awardee institution and all other participating institutions have approved Assurances on file with OPRR, and the awardee institution has provided verification of approval by the IACUC of those components of the application or proposal related to the care and use of animals. If any one of these institutions does not have an approved Assurance on file with OPRR, the awarding unit will ask OPRR to negotiate an Assurance with the institution(s) before an award is made. No award shall be made until all required Assurances have been submitted by the institution(s), been approved by OPRR, and the institution(s) have provided verification of approval by the IACUC of those components of the application or proposal related to the care and use of animals.

### **C. Conduct of Special Reviews/Site Visits**

Each awardee institution is subject to review at any time by PHS staff and advisors, which may include a site visit, in order to assess the adequacy or accuracy of the institution's compliance or expressed compliance with this Policy.

### **D. Waiver**

Institutions may request a waiver of a provision or provisions of this Policy by submitting a request to OPRR. No waiver will be granted unless sufficient justification is provided and the waiver is approved in writing by OPRR.



## FOOTNOTES

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### Footnote 1:

Assurances should be sent to the Division of Animal Welfare, Office for Protection from Research Risks, National Institutes of Health, 6100 Executive Boulevard, MSC 7507, Suite 3B01, Rockville, Maryland 20892-7507. The address for express or hand-delivered mail is Division of Animal Welfare, Office for Protection from Research Risks, National Institutes of Health, 6100 Executive Boulevard, Suite 3B01, Rockville, Maryland 20852.

### Footnote 2:

This Policy requires that Assured institutions base their programs of animal care and use on the *Guide for the Care and Use of Laboratory Animals* and that they comply with the regulations (9 CFR, Subchapter A) issued by the U.S. Department of Agriculture (USDA) under the Animal Welfare Act. The *Guide* may differ from USDA regulations in some respects. Compliance with the USDA regulations is an absolute requirement of this Policy.

### Footnote 3:

The name Institutional Animal Care and Use Committee (IACUC) as used in this Policy is intended as a generic term for a committee whose function is to ensure that the care and use of animals in PHS-conducted or supported activities is appropriate and humane in accordance with this Policy. However, each institution may identify the committee by whatever name it chooses.

### Footnote 4:

As of the 1996 reprint of this Policy, the only accrediting body recognized by PHS is the American Association for Accreditation of Laboratory Animal Care (AAALAC).

### Footnote 5:

The Health Research Extension Act of 1985 requires the IACUC to be appointed by the chief executive officer (CEO) of the entity for which the committee is established. OPRR considers the CEO to be the highest operating official of the organization (such as the President of a University). If the CEO delegates authority to appoint the IACUC then the delegation must be specific and in writing. The CEO may or may not be the Institutional Official as defined by this Policy (see definition at III.G.).

### Footnote 6:

This Policy requires that Assured institutions base their programs of animal care and use on the *Guide for the Care and Use of Laboratory Animals* and that they comply with the regulations (9 CFR, Subchapter A) issued by the U.S. Department of Agriculture (USDA) under the Animal Welfare Act. The *Guide* may differ from USDA regulations in some respects. Compliance with the USDA regulations is an absolute requirement of this Policy.

### Footnote 7:

The Institutional Animal Care and Use Committee (IACUC) may, at its discretion, determine the best means of conducting an evaluation of the institution's programs and facilities. The IACUC may invite ad hoc consultants to assist in conducting the evaluation. However, the IACUC remains responsible for the evaluation and report.

### Footnote 8:

This Policy requires that Assured institutions base their programs of animal care and use on the *Guide for the Care and Use of Laboratory Animals* and that they comply with the regulations (9 CFR, Subchapter A) issued by the U.S. Department of Agriculture (USDA) under the Animal Welfare Act. The *Guide* may differ from USDA regulations in some respects. Compliance with the USDA regulations is an absolute requirement of this Policy.



**Footnote 9:**

Journal of the American Veterinary Medical Association (JAVMA), 1993, Vol. 202, No. 2, pp. 229-249, or succeeding revised editions.

**Footnote 10:**

This Policy requires that Assured institutions base their programs of animal care and use on the *Guide for the Care and Use of Laboratory Animals* and that they comply with the regulations (9 CFR, Subchapter A) issued by the U.S. Department of Agriculture (USDA) under the Animal Welfare Act. The *Guide* may differ from USDA regulations in some respects. Compliance with the USDA regulations is an absolute requirement of this Policy.

**Footnote 11:**

This Policy requires that Assured institutions base their programs of animal care and use on the *Guide for the Care and Use of Laboratory Animals* and that they comply with the regulations (9 CFR, Subchapter A) issued by the U.S. Department of Agriculture (USDA) under the Animal Welfare Act. The *Guide* may differ from USDA regulations in some respects. Compliance with the USDA regulations is an absolute requirement of this Policy.

# Professional Guidelines





# Guidelines Bibliography

American Psychological Association Committee on Animal Research and Ethics (1994). **Guidelines for ethical conduct in the care and use of animals.** Available at <http://www.apa.org/science/anguide.html>

Descriptors: justification of research, personnel, care and housing of animals, acquisition of animals, experimental procedures, euthanasia, field research, educational use of animals.

American Society of Ichthyologists and Herpetologists, The Herpetologists' League, and Society for the Study of Amphibians and Reptiles (1997). **Guidelines for use of live amphibians and reptiles in field research.** Charleston, South Carolina: American Society of Ichthyologists and Herpetologists. Available at <http://www.utexas.edu/depts/asih/pubs/herpcoll.html>

Descriptors: general considerations, IACUCs, collecting, restraint and handling, marking, housing and maintenance at field sites, disposition following studies, references.

American Society of Ichthyologists and Herpetologists, American Fisheries Society, and American Institute of Fisheries Research Biologists (1988). **Guidelines for use of fishes in field research.** Fisheries 13(2): 16-23. Available at <http://www.utexas.edu/depts/asih/pubs/fishguide.html>

Descriptors: general considerations, IACUCs, collecting, restraint and handling, marking, housing and maintenance at field sites, disposition following studies, references.

American Society of Mammalogists Animal Care and Use Committee (1998). **Guidelines for the capture, handling, and care of mammals as approved by the American Society of Mammalogists.** *Journal of Mammalogy* 79(4): 1416-1431. Available at [http://asm.wku.edu/committees/animal\\_care\\_and\\_use/ancarecomm.html](http://asm.wku.edu/committees/animal_care_and_use/ancarecomm.html)

NAL call number: 410 J823

Descriptors: background and history, field work in mammalogy, why mammalogists collect specimens, what is an adequate sample, sampling in threatened habitats, compliance with laws and regulations, methods for collecting specimens, live-trapping and netting, kill-trapping and shooting, methods for sampling tissues from live animals, responsibility for dependent offspring, social interactions, methods of euthanasia, methods for marking and tracking, holding and transporting captive animals, maintenance of wild-caught individuals in captivity, releasing previously captured live animals, health precautions.

Brown, M.J., P.T. Pearson, and F.N. Tomson (1993). **Guidelines for animal surgery in research and teaching. AVMA Panel on Animal Surgery in Research and Teaching, and the ASLAP (American Society of Laboratory Animal Practitioners).** *American Journal of Veterinary Research* 54 (9): 1544-1559.

Descriptors: anesthesia standards, intraoperative care standards, postoperative care standards, preoperative care standards, research methods, surgery, education, veterinary standards.

Canadian Council on Animal Care (1999). **CCAC guidelines on: Choosing an appropriate endpoint in experiments using animals for research, teaching, and testing: Guiding principles.**

Ottawa, Ontario, Canada: Canadian Council on Animal Care. Available at

<http://www.ccac.ca/english/gdlines/endpts/app1to8.htm>

Descriptors: animal observation, significant indicators of pain and distress, scoring significant behavioral and physiological observations to set endpoints, pilot studies to determine appropriate endpoint, determining frequency of observations, defining responsibility for observations, training personnel in clinical animal observations, role of the IACUC, monoclonal antibody production, cancer research, toxicology, pain research, infectious disease studies, vaccine trials, animal models with potential for significant levels of pain and distress, species specific signs of pain and distress, information sources, understanding normal animal behavior, recognition and assessment of pain and distress,



laboratory animals, fish, farm animals, examples of observational checklists used to determine endpoints.

- Canadian Council on Animal Care (1999). **CCAC guidelines on: training of institutional animal users**. Ottawa, Ontario, Canada: Canadian Council on Animal Care. Available at <http://www.ccac.ca/english/gdlines/draft/training.htm>  
Descriptors: philosophy of an animal user training program, course design, resource material, access to the training program, performance evaluation, recommended syllabus for an institutional animal user training program.
- Canadian Council on Animal Care (1997). **CCAC guidelines on: animal use protocol review, 1997**. Ottawa, Ontario, Canada: Canadian Council on Animal Care. Available at <http://www.ccac.ca/english/gdlines/protocol/protgde.htm>  
Descriptors: general principles, potential benefit of the research, replacement alternatives, animal model selection, reduction of animal use/numbers, refinement of experimental technique, setting endpoints, physical restraint, invasive/stressful procedures, euthanasia, hazardous materials, teaching protocols, wildlife field studies, reading list.
- Canadian Council on Animal Care (1997). **CCAC guidelines on: transgenic animals, 1997**. Ottawa, Ontario, Canada: Canadian Council on Animal Care. Available at <http://www.ccac.ca/english/gdlines/transgen/transgen1.htm>  
Descriptors: methods used for production, investigator and animal care committee responsibilities, education, proposals to create new strains, proposals to use existing strains, accounting, containment, other regulations, reading list.
- DeNardo, D. (1995). **Amphibians as laboratory animals**. *ILAR Journal* 37(4): 173-181.  
NAL call number: QL55 A1I43  
Descriptors: overview of species, anurans, frogs, salamanders, caecilians, vendors, captive breeding, field collection, importation, shipping, animal welfare regulations and policies, husbandry and housing, caging, heating, ventilation, and air conditioning, lighting, diet, water quality, sanitation, maintenance in the field, safety considerations, toxins, zoonoses, use in research, identification techniques, cage numbering, pattern marking, toe-clipping, tattooing and dye injecting, branding, tagging, transponder implantation, anesthesia--chemical, gas, hypothermia, surgery, euthanasia--physical and chemical methods.
- DeTolla, L.J., S. Srinivas, B.R. Whitaker, C. Andrews, B. Hecker, A.S. Kane, and R. Reimschuessel (1995). **Guidelines for the care and use of fish in research**. *ILAR Journal* 37(4): 159-173.  
NAL call number: QL55 A1I43  
Descriptors: principal investigator, animal care personnel, IACUC members, overview of current uses of fish in research and commerce, marine and freshwater species used in research, factors to consider when determining choice of species, vendors, ease of maintenance, space, sources of fish, state and federal permits and licenses, summary of applicable animal welfare laws and guidelines, developing procedures for housing, husbandry, and breeding, centralized facilities, construction materials, water quality, diet, temperatures, illumination, pH, salinity, alkalinity, and hardness, dissolved oxygen, nitrogen, artificial sea water, shipping, acclimation, quarantine, research laboratories, dangerous aquatic animals and safety conditions, traumatogenic animals, venomous fish, electrogenic animals, zoonoses, examples of uses of species in biomedical research, anesthesia, analgesia, and euthanasia--overview of available agents, IACUC protocol review.
- Federation of Animal Sciences Societies (1999). **Guide for the care and use of agricultural animals in agricultural research and teaching**. Savoy, Illinois: Federation of Animal Sciences Societies, 120 p.  
NAL call number: QL55 G8 1999

Descriptors: institutional policies, general guidelines for animal husbandry, animal health care, physical plant, beef cattle husbandry, dairy cattle husbandry, horse husbandry, poultry husbandry, sheep and goat husbandry, swine husbandry, veal calf husbandry, zoonotic diseases, anesthesia and analgesia, euthanasia, organizations.

Gaunt, A.S., L.S. Oring, K.P. Able, D.W. Anderson, L.F. Baptista, J.C. Barlow, and J.C. Wingfield (1999). **Guidelines to the use of wild birds in research**. Washington, D.C.: The Ornithological Council. Available at

<http://www.nmnh.si.edu/BIRDNET/GuideToUse/index.html>

Descriptors: IACUCs, permits, investigator impact, collecting and trapping, marking, transport, housing and captive breeding, major and minor manipulative procedures, anesthesia, euthanasia, code of ethics.

Greene, H.W. (1995). **Nonavian reptiles as laboratory animals**. *ILAR Journal* 37(4): 182-186.

NAL call number: QL55 A1I43

Descriptors: overview of species, composition, characteristics, and uses in research, species availability, vendors, captive breeding, field collection, shipping, husbandry and housing, heating, ventilation, lighting, air conditioning, diet, sanitation, safety considerations, toxins and other weaponry, zoonoses, identification techniques, anesthesia, euthanasia, surgery, animal welfare regulations and policies, behavioral complexity, ethical issues.

**Guiding Principles for the Care and Use of Animals in the Field of Physiological Sciences**

(1990). *Journal of the Physiological Society of Japan* 52(1): 27-29.

Descriptors: human, animal welfare, research, ethics, ACUC.

Health Canada (1996). **Laboratory Biosafety Guidelines**. Ottawa, Ontario: Health Protection Branch, Laboratory Centre for Disease Control. Available at

<http://www.hc-sc.gc.ca/hpb/lcdc/biosafety/docs/index.htm>

Descriptors: introduction, containment of biohazards, regulations, classification of biological agents according to risk, physical containment levels, large scale production of microorganisms, laboratory design, safety equipment, safety cabinets, fume hoods, filtration systems, bibliography, glossary.

Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council (1996). **Guide for the Care and Use of Laboratory Animals, 7th Ed.** Washington, D.C.:

National Academy Press, 125p. Available at <http://books.nap.edu/html/labrats/>

NAL call number: SF406.G95 1996.

AB- Incorporates recent research on commonly used species, including farm animals. Covers institutional policies and responsibilities, animal environment, husbandry, and management, veterinary care, and physical plant.

Descriptors: alternatives, laboratory animals, U.S. Public Health Service, laboratories, animal husbandry, veterinary care.

Institute of Laboratory Animal Resources (1991). **Education and Training in the Care and Use of Laboratory Animals: A Guide for Developing Institutional Programs**. National Academy of Sciences, Committee on Educational Programs in Laboratory Animal Science, Washington, DC: National Academy Press, 139 pp.

NAL call number: SF604.E3

Descriptors: laboratory animals, animal welfare, training, bibliography.

Institute of Laboratory Animal Resources (1990). **Guia Para el Cuidado y uso de Animales de Laboratorio. Revisada en 1985. Translation of: Guide for the Care and Use of Laboratory Animals NIH publication no. 90-23S**. Committee on Care and Use of Laboratory Animals, U.S. Department of Health and Human Services, Public Health Service, Bethesda, Maryland: National Institutes of Health, 83 pp.



NAL call number: SF406.G8 1990

Descripciones: animales del laboratorio, bienestar de animales, entrenamiento, bibliografía.

Jackson, L.R. and J.G. Fox (1995). **Institutional policies and guidelines on adjuvants and antibody production.** *ILAR Journal* 37(3): 141-152.

NAL call number: QL55 A1I43

Descriptors: summary of policies from 30 facilities in the United States, monoclonal antibodies, selection of animals, immunization protocols, priming agents, inoculation of hybridoma cells, abdominal paracentesis, clinical observations, alternatives, polyclonal antibodies, selection of animals, antigen preparation, antigen-adjuvant emulsions, Freund's adjuvants and alternatives, injection site selection and preparation, routes, volumes, and sites of administration, post-injection observations, blood collection, restraint, institutional resources, personnel safety.

Jackson, R.K. (1997). **Unusual laboratory rodent species: Research uses, care and associated biohazards.** *ILAR Journal* 38(1): 13-21.

NAL call number: QL55 A1I43

Descriptors: wild rodent species, voles, deer mice, cotton rats, ground squirrels, trumpet-tailed rats or degus, multimammate rat, woodchucks, uses in research, special husbandry considerations, potential zoonoses and biohazards.

National Institutes of Health (1992). **Using Animals in Intramural Research, Guidelines for Investigators.** Bethesda, Maryland: NIH Animal Care and Use Committee.

NAL call number: HV4928.U84 1992.

Descriptors: laboratory animals, animal experimentation, animal welfare.

National Institutes of Health (1994). **Using Animals in Intramural Research, Guidelines for Investigators and Guidelines for Animal Users.** Bethesda, Maryland: NIH Animal Research Advisory Committee, Office of Animal Care and Use.

NAL call number: HV4928.U85 1994.

Descriptors: animal experimentation, laboratory animals, animal welfare, federal guidelines.

National Institutes of Health (1992). **Institutional Animal Care and Use Committee Guidebook, NIH Publication no. 92-3415.** Washington, D.C.: U.S. Government Printing Office.

NAL call number: HV4764.I58 1992.

Descriptors: laboratory animals, animal experimentation, animal welfare.

Pough, H. (1992). **Recommendations for the care of amphibians and reptiles in academic institutions.** Washington, D.C.: National Academy Press. Available at

<http://netvet.wustl.edu/species/reptiles/pough.txt>

Descriptors: research and teaching, biology, physical environment, biological environment, marking, breeding, environmental conditions, medical care, health precautions for release of animals, health precautions for caretakers.

Rehg, J.E. and L.A. Toth (1998). **Rodent quarantine programs: Purpose, principles, and practice.** *Laboratory Animal Science* 48(5): 438-447.

NAL call number: 410.9 P94

Descriptors: animal health assessment, likelihood of dispersion of microorganisms of interest throughout the quarantine population during the quarantine period, interval necessary for exposed rodents to undergo seroconversion or for microorganisms to reach detectable numbers, principles of an effective program, passive vs active programs, confidence level of detection, risk of infection, cost, scientific considerations, type of caging, type of secondary enclosure, sentinel exposure method, target organisms, quarantine programs in practice, overview of program at St. Jude Children's Research Hospital, vendor specifications, sources of infection for rodents.

Secord, D.C. and H.C. Rowsell (1974). **Proper use of animals in schools: An educational program.** *Canadian Veterinary Journal* 15(2):42-47.  
NAL call number: 41.8 R3224  
Descriptors: biology programs, animal care, guidelines, ACUC.

Stokes, W.S. and D.J.B. Jensen (1995). **Guidelines for institutional animal care and use committees: consideration of alternatives.** *Contemporary Topics in Laboratory Animal Science* 34 (3):51-55, 58-60.  
NAL call number: SF405.5.A23.  
Descriptors: animal testing alternatives, committees, guidelines, information services, training, regulations.

## Useful World Wide Web Sites

### **Institutional Animal Care and Use Committee Guidebook**

[http://grants.nih.gov/grants/oprr/iacuc\\_guidebook/iacuc\\_guidebook.htm](http://grants.nih.gov/grants/oprr/iacuc_guidebook/iacuc_guidebook.htm)

### **Guide for the Care and Use of Laboratory Animals**

<http://www.nap.edu/readingroom/books/labrats/>

### **Tutorial on the PHS Policy on Humane Care and Use of Laboratory Animals**

<http://grants.nih.gov/grants/oprr/tutorial/index.htm>

### **Sample Documents for Implementation of the PHS Policy on Humane Care and Use of Laboratory Animals**

<http://grants.nih.gov/grants/oprr/sampledoc/index.htm>

### **National Institutes of Health Animal Research Advisory Committee Guidelines**

<http://oacu.od.nih.gov/ARAC/index.htm>

This site includes: (1) guidelines for NIH intramural research program compliance with USDA annual reporting requirements, revised 4/09/97; (2) definitions and behavioral/clinical signs of pain; (3) guidelines on classifying deficiencies identified during semiannual reviews, revised 1/13/99; (4) guideline regarding significant changes to animal study proposals, revised 12/9/98; (5) NIH animal transportation guidelines, revised 2/10/99; (6) NIH animal transfer agreement, 2/12/97; (7) guidelines for housing animals in containment housing systems, reapproved 1/13/99; (8) NIH intramural position paper - "housing multiple species of large laboratory animals", revised 1/13/99; (9) guidelines for diet control in behavioral studies, reapproved 2/10/99 (10) Interagency Research Animal Committee (IRAC) recommendation on LD50 testing, reapproved 5/8/96 (11) NIH intramural research program - guidelines for survival rodent surgery, reapproved 2/10/99; (12) oocyte harvesting in *Xenopus laevis*, revised 2/10/99; (13) NIH intramural program guidelines for the prevention and control of tuberculosis in nonhuman primates, reapproved 2/10/99; (14) Interagency Research Animal Committee recommendations on toe clipping of animals, reapproved 5/8/96; (15) ascites production in mice, revised 3/11/98; (16) endpoints in animal study proposals, reapproved 2/10/99; (17) 1993 report of the AVMA panel on euthanasia, 1/15/93; (18) guidelines for the euthanasia of mouse and rat fetuses and neonates, revised 11/10/98; (19) minimum requirements for protective clothing in animal facilities, reapproved 2/10/99.





# World Wide Web Resources





Because World Wide Web Resources are most easily accessed via computer, this listing will mainly include web addresses of sites that serve as clearinghouses for specific topics. Selected web sites from universities that provide comprehensive listings of institutional policies, guidelines, and forms are also included. Other web sites may be found in each chapter; organizational websites will be found in the Organizations chapter.

### **Altweb**

<http://altweb.jhsph.edu/>

Altweb is a site for news, information, discussion, and resources from the field of alternatives to animal testing. This site is a collaborative effort funded by the Alternatives Research & Development Foundation, the Doerenkamp - Zbinden Foundation, the Humane Society of the United States, the Office for Protection from Research Risks at the National Institutes of Health, and the Procter & Gamble Company. It is being developed by the Center for Alternatives to Animal Testing at Johns Hopkins University, in collaboration with the Altweb Project Team, to serve academic, industrial and government scientists, educators, the media, and the general public.

Altweb is intended to foster the development of scientifically acceptable in vitro and other alternatives to animal testing. Alternatives are defined as methods which reduce animal use, replace whole animal tests, or refine existing tests by minimizing animal distress.

Need help locating alternatives databases or funding sources? Check out Science & Regulations. Want to learn about the latest software and other computer resources available for your junior high? See Educational Resources. Want to know more about the history of the alternative movement? See General information.

### **Animal Care, USDA, Animal and Plant Health Inspection Service**

<http://www.aphis.usda.gov/reac/>

This site provides access to the USDA agency that administers two laws that seek to ensure the humane handling of animals: the Animal Welfare Act (AWA) and the Horse Protection Act (HPA). Included are:

- ★ full-text versions of the Animal Welfare Act and the Horse Protection Act, USDA animal welfare regulations, standards, and policies;
- ★ Annual report to Congress;
- ★ lists of licensed or registered research facilities, dealers, breeders, carriers, and exhibitors;
- ★ fact sheets and other miscellaneous information;
- ★ Freedom of Information records;
- ★ publications; and
- ★ Missing Pet Network.

### **Animal Welfare Information Center (AWIC), United States Department of Agriculture (USDA)**

<http://www.nal.usda.gov/awic/>

This site provides access to:

- ★ full-text versions of all pertinent Federal laws, regulations, guidelines and policies, and links to international laws;
- ★ AWIC newsletters;
- ★ AWIC publications;
- ★ links to databases, information on alternatives, farm animals, and organizations;
- ★ links to the National Agricultural Library, Animal and Plant Health Inspection Service, Office for Protection from Research Risks, and NetVet.



## **Compilation of Literature on the Assessment of Animal Welfare and Animal Distress**

<http://www.vetinfo.demon.nl/aw/>

Extensive bibliography and links to full-text documents related to the assessment of pain in animals, animal welfare, and animal distress. Produced by dr. J.D. Kuiper, Department of Laboratory Animal Sciences, Utrecht University, The Netherlands, and Tim Allen, Animal Welfare Information Center, U.S. Department of Agriculture.

## **Institute of Laboratory Animal Resources Journal**

<http://www4.nas.edu/cls/ijhome.nsf>

ILAR Journal is the quarterly, peer-reviewed publication of the Institute for Laboratory Animal Research (ILAR), which is a unit of the National Research Council, National Academy of Sciences. ILAR Journal provides thoughtful and timely information for all those who use, care for, and oversee the use of laboratory animals. Provides access to online version of the journal and many back issues; a searchable index is available.

## **IACUC Training and Learning Consortium (IACUC TLC)**

<http://www.iacuc.org/>

Few people know it, but the idea for this site was first proposed by Ken Boschert several years ago. The site has been developed and maintained under the direction of Nicole Duffee, DVM, Washington University. The IACUC Training and Learning Consortium Task Force is an ad hoc committee established by the American Association for Laboratory Animal Science (AALAS) with the charges:

- ★ To produce a comprehensive core course to train IACUC members.
- ★ To develop, design and provide oversight for this IACUC training course.
- ★ To develop, design and provide oversight for a Web site ([www.iacuc.org](http://www.iacuc.org)) for comprehensive information and resources on all matters pertaining to IACUCs.
- ★ To establish a listerv (IACUC-FORUM) for IACUC members and staff to encourage dynamic information exchange on the IACUC process.
- ★ To establish an advisory group representing a national consortium of organizations with shared interest in the education and training of IACUC members to jointly sponsor the IACUC training initiative, with AALAS coordinating the effort.

This site provides access to:

- ★ General Information | Listserv | Partners;
- ★ Alternatives;
- ★ Bibliography of IACUC Topics, Databases, Example Forms and Documents;
- ★ Laws, Policies, Guidelines and Other Documents;
- ★ Institutional Research Policies and Procedure Guidelines;
- ★ Journals and Publications, Meetings, and Organizations;
- ★ Training - IACUC members; and
- ★ Training - Laboratory Animal Care and Use.

## **Intramural Animal Care and Use (ACU) program of the National Institutes of Health (NIH)**

<http://oacu.od.nih.gov/index.htm>

Although this page is intended to serve as an information resource for NIH scientists, Animal Care and Use Committee (ACUC) members, veterinarians, animal science specialists, and other NIH staff involved in the conduct of biomedical research at NIH, the information presented is certainly of use to other animal care and use committees. A very well-done site.

## Lab Animal IACUC Resource Page

<http://www.labanimal.com>

This site is provided by *Lab Animal* magazine and contains the following:

- ★ IACUC Reading Room—Recent Lab Animal articles for the IACUC member. Browse article selections, and enjoy full-text access in either PDF or HTML formats.
- ★ Protocol Review—Jerry Silverman's popular "Protocol Review" column. Join your colleagues in resolving "Great Eastern University's" IACUC quandaries. Perfect for training, or simply honing your review skills.
- ★ Regulatory Updates
- ★ IACUC-Related Links
  - IACUC Resources on the Web
  - Alternatives
  - Databases & Search Functions
  - Endpoints & Pain Management
  - Literature Search for Alternatives (USDA Policy 12)
  - Pain & Distress
  - Regulations and Policies
  - Training

## Massachusetts Society for Medical Research (MSMR)

<http://www.msmr.org/resource.html>

This site provides access to the MSMR Nation-Wide Resources List - an interactive listing of state biomedical research organizations and national organizations that promote biomedical research. To access the home page of MSMR, click on the Home Page icon at the bottom of the page.

## National Agricultural Library's (NAL) Web Gateway to AGRICOLA (AGRICultural OnLine Access)

<http://www.nal.usda.gov/ag98/>

AGRICOLA (AGRICultural OnLine Access) is a machine-readable database of bibliographic records created by the National Agricultural Library and its cooperators. Production of these records in electronic form began in 1970, but the database covers materials dating from the 16<sup>th</sup> century to the present. The records describe publications and resources encompassing all aspects of agriculture and allied disciplines, including plant and animal sciences, forestry, entomology, soil and water resources, agricultural economics, agricultural engineering, agricultural products, alternative farming practices, and food and nutrition. Auxiliary subjects that support NAL's Information Center activities, such as agricultural trade and marketing, rural information, and animal welfare, are also included.

## National Library of Medicine—MEDLINE: PubMed and Internet Grateful Med

<http://www.nlm.nih.gov/databases/freemedl.html>

NLM offers PubMed and Internet Grateful Med, two free systems to search MEDLINE. They:

- ★ Provide an easy way to search the 11 million references and abstracts in the MEDLINE database;
- ★ Use PubMed's retrieval engine to link to about 400 journals for full text of articles (some publishers may require a subscription) and provide pre-computed sets of relevant MEDLINE articles;
- ★ Offer NLM's Medical Subject Headings for searching; and
- ★ Use Loansome Doc for document delivery services (there may be local charges).

## **NetVet Veterinary Resources and the Electronic Zoo**

<http://netvet.wustl.edu/>

Perhaps the Web's most comprehensive listing of animal-related web sites, NetVet & the Electronic Zoo were created by Ken Boschert, DVM, at Washington University's Division of Comparative Medicine, located in St. Louis, Missouri. Among this server's Web Pages are numerous views of Veterinary Medical and Animal resources available on the Internet and beyond. Topics include: What's New, a site Search engine, Career information, Education, Veterinary Specialties, Organizations, Meetings, E-Lists, Publications, Images, Government, Commerce, ElectronicZoo.

## **Office for Protection from Research Risks (OPRR), NIH Office of Extramural Research**

<http://grants.nih.gov/grants/oprr/oprr.htm#LAB>

This site provides access to the NIH agency that administers animal welfare assurances of Public Health Service fundholders. Information provided includes:

- ★ Public Health Service Policy on Humane Care and Use of Laboratory Animals, March, 1996
- ★ 1996 Guide for the Care and Use of Laboratory Animals, National Academy of Sciences
- ★ Health Research Extension Act of 1985, Public Law 99-158, November 20, 1985, Section 495, "Animals in Research"
- ★ Tutorial on the PHS Policy on Humane Care and Use of Laboratory Animals
- ★ Sample Documents for Implementation of the PHS Policy on Humane Care and Use of Laboratory Animals
- ★ Institutional Animal Care And Use Committee Guidebook, ARENA
- ★ World Wide Web Resources for the IACUC - an excellent compilation of sites providing useful IACUC information.

## **University IACUC Sites**

### **Arizona State University, Animal Care and Use**

[http://researchnet.asu.edu/animal\\_care/](http://researchnet.asu.edu/animal_care/)

### **Florida State University Laboratory Animal Program**

<http://mailer.fsu.edu/~FSULAR/home.html>

### **University of Arizona Institutional Animal Care and Use Committee Handbook**

<http://www.ahsc.arizona.edu/uac/iacuc/>

### **University of California, Irvine—Animal Subjects**

<http://www.rgs.uci.edu/rig/asindex.htm>

### **University of Colorado Health Sciences Center Animal Care & Use Program**

<http://www.uchsc.edu/sm/animal/index.html>

### **University of Florida Animal Care & Use**

<http://nersp.nerdc.ufl.edu/~iacuc/index.html>

### **University of Minnesota, Research Animal Resources**

<http://www.ahc.umn.edu/rar/>

### **University of Nebraska-Lincoln, Institutional Animal Care and Use Committee**

<http://www.unl.edu/research/ReComp/IACUC/iacuctoc.htm>

### **University of Tennessee - Knoxville (UT-K), Office of Laboratory Animal Care**

<http://www.ra.utk.edu/ora/labaniml/>

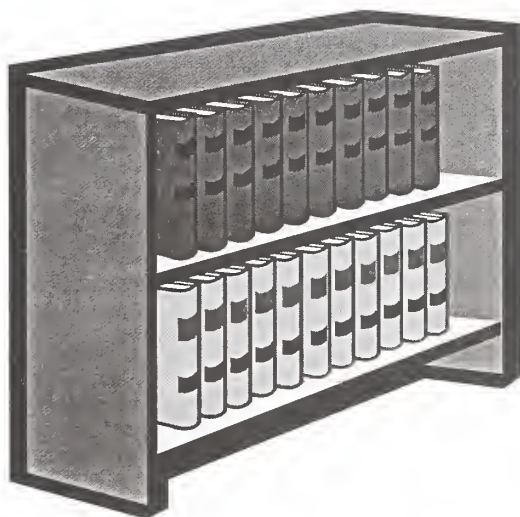
# Articles and Bibliographies







# General





# The Institutional Animal Care and Use Committee (IACUC)

(Excerpted from National Institutes of Health (1992). *Institutional Animal Care and Use Committee Guidebook*, NIH Publication no. 92-3415. Washington, D.C.: U.S. Government Printing Office.) The full text of this document may be found at [http://grants.nih.gov/grants/oprr/iacuc\\_guidebook/iacuc\\_guidebook.htm](http://grants.nih.gov/grants/oprr/iacuc_guidebook/iacuc_guidebook.htm)

## A-2. Authority, Composition and Functions

Each institution which falls under authority of the AWA and/or receives PHS support for research and teaching involving laboratory animals must operate a program with clear lines of authority and responsibility, a properly functioning Institutional Animal Care and Use Committee (IACUC), procedures for self monitoring, adequate veterinary care, a program of occupational health, sound animal husbandry practices, and appropriate maintenance of facilities for housing animals.

The IACUC also monitors the use of animals in teaching activities as specified in the USDA Regulations, but this does not come under the Policy, unless it is supported by PHS.

The IACUC must have at least five members, including a veterinarian with program responsibilities, a scientist experienced in laboratory animal research, a non-scientist and an individual who has no other affiliation with the Institution besides membership in the IACUC. The IACUC must have the full support of the Institutional Official responsible for the program; evaluate the entire program every six months; prepare a report on the evaluation and the inspection of the facilities which is to be filed with the Institutional Official; and make recommendations to this Official concerning deficiencies, with a proposed timetable for corrections. The IACUC has the authority to suspend PHS-supported research activities.

The IACUC has an obligation to review all research projects, proposed for PHS support, prior to their receiving funding. A written report of this review confirms that the project will be conducted in accordance with PHS Policy, the Guide and the AWA. At least one member of the Committee must review each proposal, but all members must have prior opportunity to request full Committee review. The IACUC has authority to approve, require modifications before approval, or withhold approval of proposals submitted to it for review. No activity involving animals can begin unless it is first approved by the IACUC.

The frequency of IACUC consideration of approved, ongoing activities is one of the few areas in which PHS and USDA have differing requirements, i.e., PHS requires it at least once every three years, whereas USDA requires it annually. Ideally, institutions should choose to establish a uniform mechanism which satisfies both federal requirements. In deliberating this issue it is helpful to refer to consideration of ongoing activities by the use of the term “annual review” as opposed to the function of the IACUC performed at the outset of a new activity and at the expiration of an approved activity, referred to as ‘review.’ OPRR has interpreted PHS Policy to require an institutional process which provides review of proposed activities, with committee approval for a specified period of time generally not to exceed three years. This “initial renewal review” and approval may be accomplished by either convened Committee action or by a “designated reviewer/expedited review” process which meets the PHS Policy requirements... During this period of approval, annual review must be accomplished to meet USDA requirements. The purpose of annual review is to confirm that no changes have taken place in the approved activity which might require further consideration by the IACUC, and to ensure that any new requirements of PHS, USDA or the institution are transmitted to the investigator. Annual review need not require a convened IACUC or designated reviewer/expedited action but must be adequately documented. Planned modifications must be brought to the attention of the IACUC prior to initiation. A relatively



simple mechanism to meet USDA requirements is the annual circulation of a standard form giving current basic IACUC information, e.g., approval number, date, title, species, etc., to all investigators with IACUC-approved activities. The investigator then notes that either no changes have taken place, or he/she describes any changes which have occurred. The IACUC may then separate responses, filing those indicating no changes and passing along the remainder to an IACUC-designee for assessment of the changes reported. Any changes to the approved activity which are deemed of sufficient magnitude to merit further consideration may then be presented to the IACUC. All of these dispositions should be documented as official IACUC actions.

### **Table I: Federally Mandated IACUC Functions**

Review, at least once every 6 months, the research facility's program, using USDA Regulation/Guide as basis.

- ★ Inspect, at least once every 6 months, all of the animal facilities, including animal study areas/satellite facilities, using USDA Regulations/Guide, as basis.
- ★ Prepare reports of IACUC evaluations and submit the reports to the Institutional Official.
- ★ Review and investigate legitimate concerns involving the care and use of animals at the research facility resulting from public complaints and from reports of non-compliance received from facility personnel or employees.
- ★ Make recommendations to the Institutional Official regarding any aspect of the research facility's animal program, facilities or personnel training.
- ★ Review and approve, require modifications in (to secure approval), or withhold approval of those components of proposed activities related to the care and use of animals.
- ★ Review and approve, require modifications in (to secure approval), or withhold approval of proposed significant changes regarding the care and use of animals in ongoing activities.
- ★ Suspend an activity involving animals when necessary; take corrective action and report to funding agency and USDA.

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Chimpanzees are more like humans than any other living beings, differing in the composition of their DNA by just over one per cent. There are striking similarities in the anatomy and wiring of the chimpanzee and human brains and central nervous systems. Thus, it should not be surprising to find that there are also striking similarities in the social behaviour, emotional needs and expressions, and cognitive abilities of chimpanzees and humans. These similarities have become increasingly apparent during the last 15 years. Chimpanzees in the wild develop close affectionate bonds between family members that may persist throughout their lifetime of 50 years or more, and examples of true altruism, when individuals protect or even save the lives of non-related companions. Chimpanzees use many objects as tools, and tool-using behaviours differ from place to place across their range. Indeed, there are a number of behaviours that vary between different groups - evidence of cultural traditions passed from one generation to the next through observational learning and imitation. Thus chimpanzees have a very special relationship with humans. A healthy adult chimpanzee is more similar to a healthy adult human in the expression of the intellect than a brain-damaged human, yet in many medical research facilities, chimpanzees are maintained in bleak, bare cages measuring only 5' X 5' X 7'. They may remain in these prisons for life. We do not treat hardened human killers so badly in our society today - there would be a public outcry if we did. I feel strongly that the use of a being so like us, as a human guinea-pig, is not morally justified, and to that end the Jane Goodall Institute has been involved in three workshops with the aim of clarifying the extent to which they are seen to be useful in diseases such as hepatitis and AIDS research. There is no consensus among scientists regarding their usefulness at the present time. If the proposed experiments of transplanting chimpanzee bone marrow tissue into AIDS patients go ahead in the Netherlands, it will be a sad blow for chimpanzee liberation. The attitude of those who believe that any use of non-human primates can be justified provided it results in some benefit, or expected benefit, to humankind, is of precisely

the same mind set as that which once allowed us to exploit human beings of another race and use them as slaves. Once we admit that chimpanzees have minds and feelings, are capable of sadness, fear and despair, are able to feel pain, show altruism, and are capable of communicating with each other and with humans in a man-made language, we have to ask serious questions, initially of ourselves, as to whether we should continue to use them in medical research.

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Descriptors: animal welfare, ethics, animal behavior, philosophy.

Jennings, M. and S. Silcock (1995). **Benefits, necessity and justification in animal research.**

*Alternatives to Laboratory Animals: ATLA* 23 (6): 828-836.

NAL call number: Z7994.L3A5.

AB- The cost-benefit assessment in the Animals (Scientific Procedures) Act 1986 is said to ensure that animals are only used in experiments which are justified and necessary. The way in which the Home Office Inspectorate derives the cost-benefit assessment is explained in the Report of the Animal Procedures Committee for 1993. However, evaluation of both costs and benefits is largely subjective, as are concepts such as "necessity" and "justification". These concepts mean different things to different people in different places and at different times, depending on the pressures to which they are subject. These include the socio-economic climate and the context in which the proposed research is to be earned out. Animal use cannot, therefore, be said to be necessary and/or beneficial unless serious questions are answered with respect to who or what the research is necessary for, who or what will benefit from it and who defines the criteria used in the justification process. Retrospective analysis of whether the proposed benefit was actually achieved and applied is also important. Discussion regarding the necessity, benefits and justification of individual research projects, and of overall research goals or directions, tends to be obscured by the polarised debate over the morality and scientific validity of animal experiments as a whole. This paper raises some of the issues that could be discussed in a wider view of the cost-benefit assessment, with reference to selected areas of animal use as examples. Descriptors: animal experiments, animal welfare, ethics, regulations.

Lehman, H. (1993). **Are value judgements inherent in scientific assessment?** *Journal of Agricultural & Environmental Ethics* 6 (special suppl.2): 60-67.

NAL call number: BJ52.5.J68.

Descriptors: values, ethics, methodology.

McCarthy, C.R. (1995). **Ethical aspects of animal-to-human xenografts.** *ILAR Journal* 37 (1): 3-8.

NAL call number: QL55.A1I43.

Descriptors: xenografts, organs, genetic engineering, transplantation, recipients, animal welfare, bioethics.



- McCarthy, C.R. (1995). **How and why should IACUC's develop a code of ethics?** In *Current Issues and New Frontiers in Animal Research*, K.A.L. Bayne, M. Greene, and E.D. Prentice, (eds.), Greenbelt, Maryland: Scientists Center for Animal Welfare, pp. 31-33.  
NAL call number: HV4913 C87 1995  
Descriptors: arguments for and against IACUC's exercising leadership in developing a code.
- Mepham, T.B. (1993). **Approaches to the ethical evaluation of animal biotechnologies.** *Animal Production*. 57 (pt.3): 353-359.  
NAL call number: 49 An55.  
Descriptors: transgenic animals, animal welfare, biotechnology, bioethics.
- Orlans, F. B. (1997). **Ethical decision making about animal experiments.** *Ethics Behavior* 7(2): 163-171.  
Descriptors: laboratory animals, ethics, research, pain, distress.
- Remfry, J. (1985). **Ethical committees and animal experimentation.** *Veterinary Record* 117(19): 508.  
NAL call number: 41.8 V641  
Descriptors: animal research, review, ethics, ACUC.
- Rodenburg, F. (1997). **The ethical use of animals in research, teaching, and testing.** *CALAS/ACSAL* 31(4): 116-119.  
NAL call number: SF405.5 C36  
Descriptors: Canadian approach to ethical review, tools for ethical analysis, Dutch model, ethical scoring system, British model, biotechnology.
- Rollin, B.E. (1993). **Animal welfare, science, and value.** *Journal of Agricultural & Environmental Ethics* 6 (special suppl.2): 44-50.  
NAL call number: BJ52.5.J68.  
Descriptors: animal welfare, zoology, pain, stress, moral values, ethics.
- Rollin, B.E. (1996). **Bad ethics, good ethics and the genetic engineering of animals in agriculture.** *Journal of Animal Science* 74(3): 535-541.  
NAL call number: 49 J82.  
AB- Genetic engineers have been remiss in addressing ethical and social issues emerging from this powerful new technology, a technology whose implications for agriculture are profound. As a consequence of this failure, society has been uneasy about genetic engineering of animals and has had difficulty distinguishing between genuine and spurious ethical issues the technology occasions. Many of the most prominent concerns do not require a serious response. On the other hand, concerns about a variety of possible risks arising from genetic engineering of animals require careful consideration and dialogue with the public. Such concerns are an admixture of ethics and prudence. A purely ethical challenge, however, hitherto not addressed, is represented by problems of animal welfare that arise out of genetically engineering agricultural animals. A principle of "conservation of welfare" is suggested as a plausible moral rule to guide such genetic engineering.  
Descriptors: animal welfare, genetic engineering, ethics, transgenic animals, risk, species differences, domestic animals.
- Russow, L-M. (1999). **Bioethics, animal research, and ethical theory.** *ILAR Journal* 40(1): 15-21.  
NAL call number: QL55 A1I43  
Descriptors: ethical theory, moral reasoning, treatment of animals within traditional ethical theory, differential treatment of humans and animals, morally relevant differences, animal rights, animal welfare, animalwell-being.



- Sideris, L., C. McCarthy, and D.H. Smith (1999). **Roots of concern with nonhuman animals in biomedical ethics.** *ILAR Journal* 40(1): 3-14.  
NAL call number: QL55 A1I43  
Descriptors: historical overview of animal protection, British origins, American origins, biomedical ethics, animal regulations, Silver Spring monkeys, University of Pennsylvania head trauma studies, 1985 amendments to the Animal Welfare Act, harmonization of Federal policies, guidelines and regulations.
- Simpson, J. (1984-85). **Animal rights re-evaluated.** *Free Inquiry* 5: 37-40.  
Descriptors: ethics, treatment, economics.
- Smith, J.A. and M. Jennings (1998). **Ethics training for laboratory animal users.** *Laboratory Animals* 32(2): 128-136.  
NAL call number: QL55.A1L3  
AB: In the UK, all applicants for licences under the Animals (Scientific Procedures) Act 1986 must receive training in ethical aspects of laboratory animal use. There is, however, considerable uncertainty about the aims, suitable content and most appropriate means of delivery of such training. In this review a series of aims for licensee training in ethics are proposed, the key content is described and possible approaches to delivering such training are critically evaluated. Ethics training, it is argued, should: (i) be rooted in practice, focusing on the practical application of the Act to licensees' own work and encouraging them to take all possible steps to reduce or resolve any moral conflicts which the work entails; (ii) promote discussion, encouraging licensees to challenge their own views and critically appraise their work; and (iii) provide the necessary theoretical background to inform and stimulate such discussion. A variety of means of generating discussion and a range of practical considerations are explored.
- Stephenson, W. (1991). **Institutional Animal Care and Use Committees and the Moderate Position.** *Between the Species* Winter: 6-8.  
NAL call number: HV4701 B4  
Descriptors: animal rights, biomedical research, ethics, justification, value.
- Sumner, L.W. (1988). **Animal welfare and animal rights.** *Journal of Medicine and Philosophy* 13:159-175.  
Descriptors: ethics, animal experimentation.
- Universities Federation for Animal Welfare (1972). **The Rational Use of Living Systems in Bio-Medical Research.** Universities Federation for Animal Welfare: Hertfordshire, UK.  
NAL call number: QL55 R37  
Descriptors: ethics, animal experimentation, utility, vaccine, transplantation, feeling, reason, consent.
- Webster, A.J.F. (1993). **Animal welfare: the five freedoms and the free market.** *BSAP occasional publication* (17): 45-49. In *The Series Analytic: Safety and Quality of Food from Animals*, J.D. Wood and T.L.J. Lawrence (eds.), Proceedings of a symposium held June 1992 at Bristol.  
NAL call number: SF5.B74.  
Descriptors: animal welfare, animal behavior, regulations.

## Useful World Wide Web Sites

### **Guidelines for Ethical Conduct in the Care and Use of Animals**

<http://www.apa.org/science/anguide.html>

Developed by the American Psychological Association's Committee on Animal Research and Ethics.

### **Center for Bioethics, University of Pennsylvania**

<http://www.med.upenn.edu/bioethics/index.shtml>

A general site devoted to bioethics.

### **National Bioethics Advisory Commission**

[http://bioethics.gov/cgi-bin/bioeth\\_counter.pl](http://bioethics.gov/cgi-bin/bioeth_counter.pl)

A government advisory body mainly concerned with research involving humans but has an interesting report on the science of animal cloning

### **National Reference Center for Bioethics Literature**

<http://www.georgetown.edu/research/nrcbl/>

The National Reference Center for Bioethics Literature (NRCBL), is a specialized collection of books, journals, newspaper articles, legal materials, regulations, codes, government publications, and other relevant documents concerned with issues in biomedical and professional ethics.

### **University of Minnesota, Research Animal Resources**

<http://www.ahc.umn.edu/rar/ethics.html>

A brief article on the ethics of animal research and the use of alternative methods.



# IACUC Administration and Program Review







# IACUC Oversight of Animal Care and Use Program

Excerpted from the *Institutional Animal Care and Use Committee Guidebook* developed by Applied Research Ethics National Association and the National Institutes of Health. NIH Publication number 92-3415. Full text available on-line at [http://grants.nih.gov/grants/oprr/iacuc\\_guidebook/iacuc\\_guidebook.htm](http://grants.nih.gov/grants/oprr/iacuc_guidebook/iacuc_guidebook.htm)

## **C-1. Policies, Procedures and Responsibilities**

### **Introduction**

Under PHS Policy and USDA Regulations, the IACUC must inspect all institutional animal facilities every six months. These inspections provide an ongoing mechanism for ensuring that the institution maintains compliance with the applicable animal care and use policies guidelines and laws. They can also benefit programs for animal care by serving an educational function for the animal care personnel, research staff and IACUC members. Also, by giving the facility personnel a prior warning, the IACUC can assist an institution to prepare for subsequent visits by outside inspectors. The interaction of an IACUC and the animal care personnel at their institution should be constructive, and not adversarial, as both ultimately share the same goals of good animal care.

### **Staffing and scheduling inspection**

The IACUC must schedule the inspections of facilities. This may be accomplished by assigning specific facilities to subcommittees which must contain at least two members as required by the USDA Regulations. No IACUC member should be excluded should he/she wish to attend a particular inspection, and additional ad hoc consultants may be used. The inspection team must have a working knowledge of the Guide and USDA Regulations in order to fully evaluate the facilities which are being inspected. Section C-2 of this Guidebook also provides general guidance in this regard. It is helpful for the team to have a prepared list of the categories to be inspected, such as sanitation, food and water provisions, animal identification, waste disposal, animal health records, environmental control, staff training, etc.

The IACUC may determine whether the supervisory personnel of various facilities should be notified of the date and time of an inspection. Advance notification allows individuals to be available to answer questions, but an unexpected visit shows the facility during usual operations.

### **Performing inspections**

An updated list of all facilities to be inspected should be maintained by the IACUC. All proposals submitted to the IACUC must contain details of all locations at which animal research is to be performed. The USDA Regulations require inspection of the centrally designated or managed animal resource facilities as well as any other animal containment facilities in which animals are kept for more than twelve hours. PHS Policy requires inspection of all surgical facilities and areas in which animals are maintained longer than 24 hours. It is helpful to keep a list of all facilities by room number, use, species and deficiencies noted in the last inspection. For satellite areas a contact person is useful. For facilities with multiple rooms, a map will assist the inspectors.

Notes should be taken throughout the visit to assist in preparation of the final report. Apparent deficiencies should be discussed with the person in charge of the facility to ensure that the team's perception of the situation is correct. In some cases an apparent deviation will be due to the experimental proposal in process, for example, withholding of food prior to surgery.

## **Documentation**

After the visit a formal report is prepared. Any deficiencies must be categorized as minor or significant. The latter is defined, by USDA Regulations and PHS Policy, as one of significant threat to animal health or safety. A plan and timetable for correction of all deficiencies must be included in the final report. All individuals to be involved in the corrections should be consulted to ensure that the plan is realistic. If the institution is unable to meet the plan, the IACUC through the Institutional Official must inform Animal and Plant Health Inspection Service (APHIS) officials within fifteen working days of the lapsed deadline. If the activity is federally funded, the relevant agency also must be informed.

The report must be reviewed and approved by a quorum of the IACUC, and in cases involving USDA Regulations, be signed by all those who accept the report. Minority views should be included in the final document. A copy is then sent to the Institutional Official and must be kept on file for a minimum of three years. It is often useful for the report to be delivered in person in order to emphasize the findings and plans for action. Annually, the institution must notify OPRR of the dates of the semiannual inspections and the dates the report was submitted to the Institutional Official.

## **Program Evaluation**

Both the PHS Policy and USDA Regulations include a requirement that semiannually the IACUC conduct an evaluation of the animal care and use program. Neither of these documents includes specific guidance regarding the mechanisms or procedures to employ in conducting this evaluation. OPRR has recommended that institutions use the Table of Contents of the Guide, exclusive of the facility and physical plant chapters, as an outline for program evaluation. The USDA Regulations refer institutions to other portions of those Regulations as a basis on which to conduct this program evaluation.

Key aspects of an animal care and use program that should be emphasized in the semiannual evaluation include IACUC functions and procedures, including proposal review practices, provisions for dealing with whistle blower" or other concerns regarding animal care and use, and the procedures employed to meet reporting requirements. In addition, the institution's occupational health program, veterinary care procedures and personnel qualification review process should be evaluated. Specific procedures to accomplish program evaluation may include presentations by appropriate individuals, e.g., the institutional veterinarian, occupational health personnel, etc. Written institutional policies such as standard operating procedures may be reviewed and modified if necessary.

Program evaluation deals principally with administrative aspects of the animal care and use program. In most instances these aspects will not change nor need to be modified with the same aspects of the facility or physical plant. Thus, when large changes are made in program aspects, a comprehensive evaluation by the committee should be conducted, while the review of that aspect six months later may be merely a brief evaluation of its implementation to date. Ongoing review of established practices allows the opportunity for institutions to detect a gradual change in practices from written procedures, thereby allowing modification of one or the other as appropriate. Institutions that are AAALAC accredited will find their pre-site visit package helpful in identifying areas for inclusion in the semiannual evaluation.

## **Occupational Health**

### **Purpose of occupational health programs**

The health of individuals working in animal care Programs is an area of institutional concern. PHS Policy and the Guide identify the need for an occupational health program for all personnel who work in laboratory animal facilities or who have substantial animal contact. The emphasis of such a

program is the prevention of illness, but it also includes provisions for early diagnosis and treatment when such illnesses occur.

### **Elements of an occupational health program**

An effective program will have the following components: 1) replacement medical evaluation; 2) periodic medical surveillance; 3) educational component; 4) provisions for treating illness or injury; and 5) provisions for consultation with other professional staff. The specific elements will be dictated by the extent and nature of the employee's exposure [see table].

**Replacement and periodic medical evaluations:** Replacement evaluations are conducted to ensure that the individual is capable of the demands and exposure of the job, and also to provide a medical reference baseline. The evaluation may include: clinical history, physical examination, spirometry, baseline tests such as TB test and serum sample collection, appropriate immunizations, educational/instructional component and appropriate feedback to the employee on all test results. Specific tests will depend on the species of animals and the nature of the procedures employed.

Periodic evaluations allow detection of early stages of disease, updating of immunizations and a re-evaluation of medical restrictions.

A uniformity in the evaluation of different individuals and the same person at different times is important to enable accurate comparisons to be made. These comparisons may allow a possible problem to be identified and corrected before it becomes a major health hazard.

### **Education**

There are ethical and legal requirements to inform individuals of health risks and precautions which affect them. This must be part of an employee's overall orientation and job training. Some institutions rely on formal courses.





# Administration and Review Bibliography

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NAL call number: 410.9 P94  
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- Bascom, R. (1997). **Developing and implementing personnel safety programs Part 1: Occupational health and safety program in a research animal facility.** *Lab Animal* 26(6): 23-26.  
NAL call number: QL55 A1L33  
Descriptors: five key institutional activities, administration support for health and safety programs, hazard recognition, institutional trends for health and safety, who is at risk, developing and implementing a work plan, control strategies, tracking program effectiveness.
- Bowman, P.J. (1991). **A flexible occupational health and safety program for laboratory animal care and use programs.** *AALAS Bulletin* 30(6): 15-17.  
NAL call number: SF405.5 A23  
Descriptors: zoonoses, PHS policy, factors likely to dictate type and degree of hazards, list of type of personnel that should be included in program, categories of risk, facets of an occupational health program—timelines for physical exams, TB skin tests, chest x-rays, immunizations, serum banking, allergies, injuries, Q Fever.
- Bowne, G.W. (1999). **Financial management in an animal research facility.** *Lab Animal* 28(1): 33-37.  
NAL call number: QL55 A1L33  
Descriptors: budget development and maintenance, cost analysis, review of major costs in an animal facility, expenditures, income, equipment and amortization, tracking and monitoring costs, Circular A-21, basic points for saving money, repairing a deficit.
- Carey, R. (1990). **Public responsibility in medicine and research conference on administration, education and the animal care committee.** *Journal of Medical Primatology* 19(1): 75-6.  
NAL call number: QL737 P9J66  
Descriptors: animal welfare, legislation and jurisprudence, laboratory animals, research, ACUC.
- Donnelly, T.M. (1996). **Hazardous chemicals and anesthetics in the laboratory animal facility.** *Lab Animal* 25(4): 39-41.  
NAL call number: QL55 A1L33  
Descriptors: list of commonly used hazardous chemicals and anesthetics, xylene, DMSO, picric acid, formaldehyde, peracetic acid, chloroform, ether, halothane, nitrous oxide, urethane, common use of each compound in the lab, hazards associated with chemicals, recommended protective action, miscellaneous information about each chemical.
- Driscoll, J.W. and T.C. Rambo (1989). **Forming an IACUC at a small institution.** In *Animal Care and Use in Behavioral Research: Regulations, Issues, and Applications* J.W. Driscoll (ed.), Beltsville, Maryland: U.S. Department of Agriculture/National Agricultural Library pp. 23-28.  
NAL call number: aHV4762 A3A64  
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NAL call number: QL55 A1L3

Descriptors: missions of an animal care program and the IACUC, animal care office, administrative support, advantages and disadvantages of separate vs combined animal care and IACUC offices, factors involved in determining the suitability of program for a facility, recommendations for an effective and efficient IACUC.

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NAL call number: 410.9 P94

Descriptors: laboratory animals, animal welfare, animal experiments, ACUC.

Gordon, B (1987). **Unique problems of animal care and use in small institutions.** *Laboratory Animal Science* 37(special issue): 127-128.

NAL call number: 410.9 P94

Descriptors: animal welfare, research institutes, animal experiments.

Green, R.J. (1997). **Developing and implementing personnel safety programs part II: Safety training and education in animal research.** *Lab Animal* 26(6): 27-29.

NAL call number: QL55 A1L33

Descriptors: management responsibility, dealing with time constraints, on-site training, providing regular updates, modular courses, maximizing class time, pre-class assignments, employee interaction, distance learning, computer-based training, top 10 training tips.

Hassall, G. (1999). **Committees and conflict resolution.** *ANZCCART News* 12(1): 1-3.

NAL call number: SF405.5 A3

Descriptors: conflict resolution, definitions, disputes, conflicts, conflict resolution continuum, mediation, skills, listening, empathizing, assertiveness, timeliness, mapping, strategies for resolving conflicts.

Herscowitz, H.B. (1987). **Institutional responsibilities.** *Laboratory Animal Science* 37(special issue): 118-119.

NAL call number: 410.9 P94

Descriptors: animal welfare, laboratory animals, ACUC.

Hiemae, K., H. Rozmiarek, J.F. Williams, J.E. LeBeau, and M. Ross (1987). **Report of a panel discussion on how to run an effective Animal Care and Use Committee.** *Laboratory Animal Science* 37(special issue): 39-44.

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Descriptors: animal welfare, animal experiments, policy, institutions.

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Descriptors: animal welfare, institutions, ACUC.

Holden, F. (1997). **Alternatives committee established at Indiana.** *The Johns Hopkins Center for Alternatives to Animal Testing Newsletter* 14(3): 6-7.

NAL call number: HV4701 J6

Descriptors: subcommittee to IACUC, communications between researchers and campus animal protectionists, monthly round table, institutional support at highest levels, membership includes—information specialists, public relations/education representative, departmental representatives, IACUC liaison, animal protectionist, veterinarian, research assistant.

- Holt, M.A. (1996). **Institutional animal care and use issues: creativity and innovation.** *The Johns Hopkins Center for Alternatives to Animal Testing Newsletter* 13(2): 12-13.  
NAL call number: HV4701.J6.  
Descriptors: animal welfare, committees, innovations.
- Institute of Laboratory Animal Resources (U.S.), Committee on Occupational Safety and Health in Research Animal Facilities (1997). **Occupational health and safety in the care and use of research animals.** Washington, DC: National Academy Press, 154 p. This document is available at <http://pompeii.nap.edu/books/0309052998/html/index.html>  
NAL call number: RC965.A6O23--1997  
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- James, M.L., L.A. Mininni, and L.C. Anderson (1995). **Establishment of an animal alternatives committee.** *Contemporary Topics in Laboratory Animal Science* 34 (3): 61-64.  
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Descriptors: animal testing alternatives, committees, programs.
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NAL call number: QL55 A1L33  
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NAL call number: HV4764 I46 1992.  
Descriptors: enrichment strategies, dogs, nonhuman primates.
- Lamborn, C. and M. Denny (1998). **Preparing for an animal rights related crisis.** *Lab Animal* 27(1): 32-35.  
NAL call number: QL55 A1L33  
Descriptors: crisis management, physical security, research and animal care policy, public relations, outsourcing your physical security program, check list for crisis preparation.
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NAL call number: QL55 A1L33  
Descriptors: automated data handling, simplified reporting capabilities, inventory control, GLP accountability, system and user management.
- McGarry, M.P., M.A. Imamovic, and D.J. Piccione. **Institutional animal care and use committee (IACUC) required facility inspections - objectives and implementation.** *Laboratory Animal Science* 37(4):544 (1987).  
NAL call number: 410.9 P94  
Descriptors: laboratory animals, public health, conference, ACUC.



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NAL call number: QL55.A1I43  
Descriptors: laboratory workers, laboratory hazards, occupational health, animal experiments.
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Descriptors: laboratory animals, animal welfare, workshop, research institutes, training, ethics, animal experiments.
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NAL call number: aHV4701.A952  
Descriptors: bioethics, animal welfare.
- Public Responsibility in Medicine and Research (1991). **Animal Care and Use Programs: Regulatory Compliance and Education in an Age of Fiscal Constraint** Public Responsibility in Medicine and Research (PRIM & R), Tufts University School of Veterinary Medicine and Tufts University School of Medicine, Boston, Massachusetts: PRIM & R, 408 pp.  
NAL call number: HV4913.A54  
Descriptors: educational material, bibliographies, animal welfare.
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NAL call number: QL55 A1L3  
Descriptors: animal welfare, physiology, breeding standards, cats, dogs, health status, swine, bacterial infections, diagnosis, data collection, mass screening, mycoses, parasitic diseases, virus diseases.
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Descriptors: organizational models, animal welfare, clinical laboratory information systems, computer networks, facility regulation and control.

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Descriptors: laboratory animals, animal experiments, policy, legislation, ACUC.
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Descriptors: laboratories, animal experiments, inspection, documentation.
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Descriptors: training, personnel, animal experiments, animal welfare, regulations, programs.
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NAL call number: QL55 A1L33  
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Descriptors: laboratory animals, animal welfare, committees, animal husbandry, policy, monitoring.
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NAL call number: aHV4762 A3A64  
Descriptors: Animal Welfare Act, ACUC, field research.
- Talham, D.J. (1997). **A computerized method for taking animal census.** *Lab Animal* 26(9): 32-35.  
NAL call number: QL55 A1L33  
Descriptors: manual systems, bar-coded systems, in-house programming, integration with billing and accounting systems, screen shots.
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NAL call number: SF405.5 A23  
Descriptors: commercial software vs. in-house development, system objectives, design and implementation, operational areas, protocol management, animal procurement, animal facility—generate delivery schedules, cage cards, receipt of animals, animal census, billing, cost accounting.
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## Useful World Wide Web Sites

### **A tutorial on the Public Health Service Policy on humane care and use of laboratory animals**

<http://grants.nih.gov/grants/oprr/tutorial/index.htm>

A tutorial for new animal care and use committee members, institutional administrators, investigators, animal care personnel, veterinarians, or others who are interested in learning about the PHS Policy on Humane Care and Use of Laboratory Animals.

### **Biosafety in Microbiological and Biomedical Laboratories (BMBL) 4th Edition HHS Publication No. (CDC) 93-8395**

<http://bmbf.od.nih.gov>

This 4<sup>th</sup> edition of the BMBL continues to specifically describe combinations of microbiological practices, laboratory facilities, and safety equipment, and recommend their use in four categories or biosafety levels of laboratory operation with selected agents infectious to humans. For sale by the Superintendent of Documents, U.S. Government Printing Office (GPO). Contact GPO by telephone between 7:30 a.m. and 4:30 p.m. EST at 1-202-512-1800, by fax at 1-202-512-2250 or on the Internet at <https://orders.access.gpo.gov/> or write to: Superintendent of Documents, U.S. GPO, Washington D.C. 20402. The stock number for this document is 017-040-00547-4.

### **Conflict Resolution in NIH Intramural Research Program**

<http://www.training.nih.gov/handbook/conflict.html>

General information on conflict resolution procedures

### **Department of Veterans Affairs, Veterans Health Administration-VA Animal Research Documents and Resources**

[http://www.emory.edu/va\\_atl/vmu/index.html](http://www.emory.edu/va_atl/vmu/index.html)

This site lists the animal care and use policies of the VA and provides access to other Federal and professional resources. Policies listed include: (1) animal facility equipment committee, VHA Handbook 1201.12; (2) M-3, Chapter 12, animal subjects in research; (3) request to use explosive agents; (4) request to use patient care area; (5) animal component of research protocol; (6) occupation health and safety guide; (7) VHA Directive 10-95-031, Department of Veterans Affairs (VA) responsibility for VA-owned research animals housed in non-VA facilities and non-VA-owned



research animals housed in VA facilities; and (8) VHA Directive 10-95-045, accreditation requirement for VA facilities conducting research using animal subjects regardless of funding source.

### **Guidelines on Classifying Deficiencies Identified During Semiannual Reviews**

<http://oacu.od.nih.gov/ARAC/deficien.htm>

This guideline is intended to expand upon the specific language in paragraph IV. B. 3. of the Public Health Service Policy on Humane Care and Use of Laboratory Animals (PHS Policy), which states: "The reports must distinguish significant deficiencies from minor deficiencies. A significant deficiency is one which, consistent with this Policy, and, in the judgement of the IACUC and the Institutional Official, is or may be a threat to the health or safety of the animals. If program or facility deficiencies are noted, the reports must contain a reasonable and specific plan and schedule for correcting each deficiency."

### **Medical Surveillance and the Biosafety Program - References**

<http://www.cdc.gov/od/ohs/biosfty/bioref.htm>

Includes a section on work with research animals.

### **Occupational Health and Safety in the Care and Use of Research Animals**

<http://books.nap.edu/books/0309052998/html/1.html>

This site provides access to this book produced by the National Academy Sciences in 1997.

### **Semiannual Program and Facility Review Checklist**

<http://www.nih.gov:80/grants/oprr/sampledoc/cheklist.htm>

This sample checklist is a tool designed to assist IACUCs in conducting thorough semiannual reviews. The sample checklist covers the major topics of the Guide, and the requirements of the PHS Policy. Endnotes are included to reference specific United States Department of Agriculture (USDA) regulatory requirements that differ from the PHS Policy.

### **Semiannual Report to the Institutional Official**

<http://www.nih.gov:80/grants/oprr/sampledoc/ioreport.htm>

This sample format may be used as a template to prepare the Semiannual Report to the Institutional Official.

### **University of California, Davis Animal Use and Care Administrative Advisory Committee**

<http://clueless.ucdavis.edu/>

A comprehensive site that includes: occupational health and safety in the care and use of research animals; protocols for animal care and use; AUCAAC policy statements; UC Davis policy & procedure manual excerpts; biosafety in animal facilities; how to order controlled substances; analgesic drug doses for laboratory animals; lab animal classes; searching the literature for alternatives to animal use; USDA inspections at Davis and other UC campuses; do you know as much as you ought to? Test yourself! and ; reference documents for researchers and others.

### **University of Colorado Health Sciences Center Animal Care & Use Program Occupational Health Program**

<http://www.uchsc.edu/sm/animal/index.html>

An excellent example of a comprehensive occupational health program. Access is found by scrolling down to Occ Health / Biohazards in the left frame of the web page.

### **University of Kansas - Lawrence Campus Occupational Health Program certification form**

[http://www.ukans.edu/~acu/forms/o\\_health.html](http://www.ukans.edu/~acu/forms/o_health.html)

### **Working Safely with Research Animals**

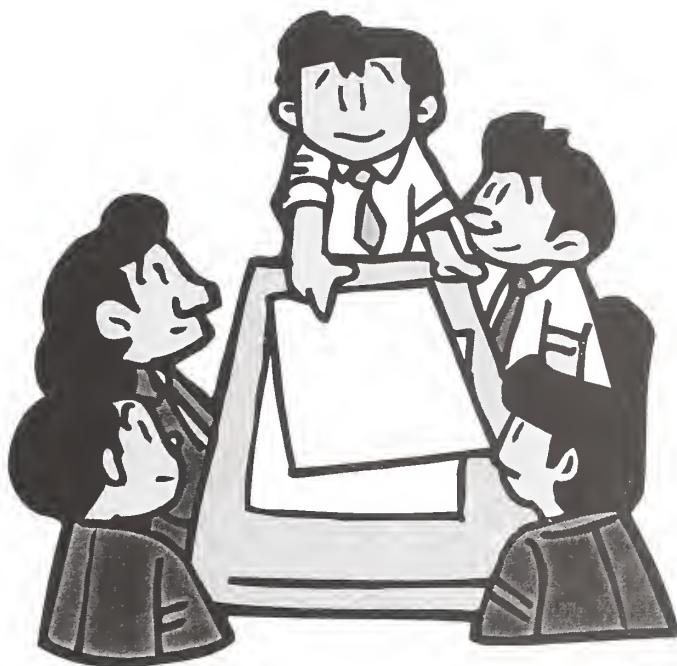
[http://www.cdc.gov/od/ohs/symposium/symp\\_idx.htm#Contents](http://www.cdc.gov/od/ohs/symposium/symp_idx.htm#Contents)

This site contains the proceedings of a conference by the Centers for Disease Control and Prevention in Atlanta, Georgia on January 27-31, 1996. The content includes: animal biosafety levels 1-4; an



overview; biosafety issues related to xenograft transplantation; sop writing; defining the risks and the risk reduction strategies; infectious risks in using baboons; xenosis from swine: assessing the infectious risks of xenotransplantation; PHS perspective on xenograft transplantation; symposium keynote: practicing safe science in animal research; biosafety and emerging infections: key issues in the prevention and control of viral hemorrhagic fevers; research with small animals; research with nonhuman primates; biohazards in research involving large animals; occupational health and safety program in a research animal facility; strategies for safe use of chemicals in animal research; chemical management in research animal facilities; physical hazards in research animal facilities; chemical containment in the animal care facility; safe practices and procedures when working with chemical hazards; zoonoses in animal care facilities; breakout session on topics including: face protection in animal research; sharps management in animal care; special containment devices for research animals; quality assurance techniques in animal facilities; strategies of managing macaque monkeys and Herpes Virus Simiae (B-virus); working safely with research animals: employee and employer responsibilities; effective management in animal research communication & interaction; occupational health programs; Americans With Disabilities Act issues; controlled access; safety training and education in animal research; risk assessment and; interactions that make OHS programs work.

# Protocol Review





# The IACUC Process: Facilitating Science in a Well-Managed Animal Care and Use Program

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The article may be found at <http://www.nal.usda.gov/awic/newsletters/v7n1/7n1ledne.htm>

## Introduction

Communication among people with diverse backgrounds and vested interests is difficult at best. This is especially true among those concerned with animal welfare issues.

An Institutional Animal Care and Use Committee (IACUC) is by its nature a focal point (fig. 1) for communication among all parties who have a stake in the use of animals in biomedical research. While each group may seek resolutions that favor its own interests, the guidepost for IACUC members, when evaluating animal use proposals, must be the ethical use of animals in research and testing.

During a typical review process, IACUC members are accustomed to hearing, "You can't do that," "You don't know the science," "You have no authority," "I've done this so many times

already," "That will take too long," "You are an impediment to research," (8). When a frustrated investigator says, "Just tell me what I need to do," an IACUC member may be tempted to respond, "You want me to do your animal use protocol for you?" Of course, that is not the intent of the process. The goal of this communication is to describe a review process by which all participants may expedite approval of an animal care and use proposal.

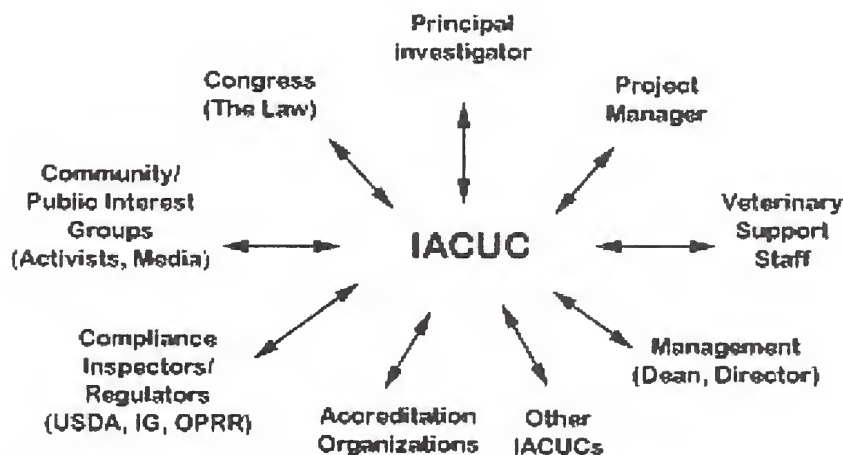


Figure 1. IACUC communication pathways



## Process Structure

It is incumbent upon each IACUC to minimize frustration by establishing a simple, practical animal care and use form and evaluation process. The participation of all staff members in initial development of the form will instill a sense of ownership of and responsibility (1) for the review process. At the same time, however, the animal care and use proposal form must be open to review and refinement as needed to handle new requirements or findings.

The IACUC form and the review process will vary according to local organizational needs and constraints. Ideally, the IACUC forms should be available on the computer (**best practice**) as well as in hard copy editions. Computer editions must be tamper proof to prevent errors of omission or commission.

The idea of a standardized animal care and use proposal form has been adopted by the Department of Defense (DoD) and may be considered by others nationwide. Standardization would enhance collaboration between organizations that share animal resources. Likewise, an institution that follows a national standard would be less open to criticism by the United States Department of Agriculture and animal rights groups.

An IACUC, according to the DoD general counsel (6), is a decision making body, not an advisory committee. Hence, appropriate attention should be given to member selection. At the Armed Forces Radiobiology Research Institute (AFRRI), service on the IACUC is voluntary. Members and alternates who represent the scientific departments are appointed by the chief laboratory officer, as are a statistician and clinical veterinarians. Two high school biology teachers represent the community (9). All IACUC members serve at the discretion of the laboratory director, and the scientific department representatives usually serve for 2 or 3 years. There are no paid administrative and secretarial staffs.

A significant strength (**best practice**) of the Institute's American Association for the Accreditation of Laboratory Animal Care (AAALAC)-accredited animal care and use program is the participation of IACUC members; executive, administrative, scientific and veterinary departmental staff; and community representatives in seminars offered by the Public Responsibility in Medicine and Research (PRIM&R), Applied Research Ethics National Association (ARENA), American Association of Laboratory Animal Science (AALAS), and Scientist's Center for Animal Welfare (SCAW). Many scientific and veterinary staff members have trained at the Animal Welfare Information Center (AWIC), in Beltsville, Maryland, to increase their computer-based bibliographic search skills. Participation at these meetings is open to all staff members and does not replace in-house training mandated by the Animal Welfare Act.

## Scientific Proposal Review Process

The IACUC proposal review process commences when an investigator conceptualizes a research idea for which internal or extramural research funds will be requested (fig. 2). Generally, a rigorous and relevant literature search (**problem area**) is conducted in order to generate a grant or scientific proposal to acquire research funds. If literature searches are limited to the National Library of Medicine CD-ROM's (Medline, Toxline, etc.) and the investigator's own holdings, the IACUC can not be assured that the proposed use of animals is not unduly redundant. Therefore, it is recommended that the investigator work with a local librarian or the AWIC staff to determine which computer-based bibliographic services should be used. Because the numerous electronic databases can be expensive to use, it is incumbent on the investigator to work with a librarian to develop a strategic approach to the bibliographic search.

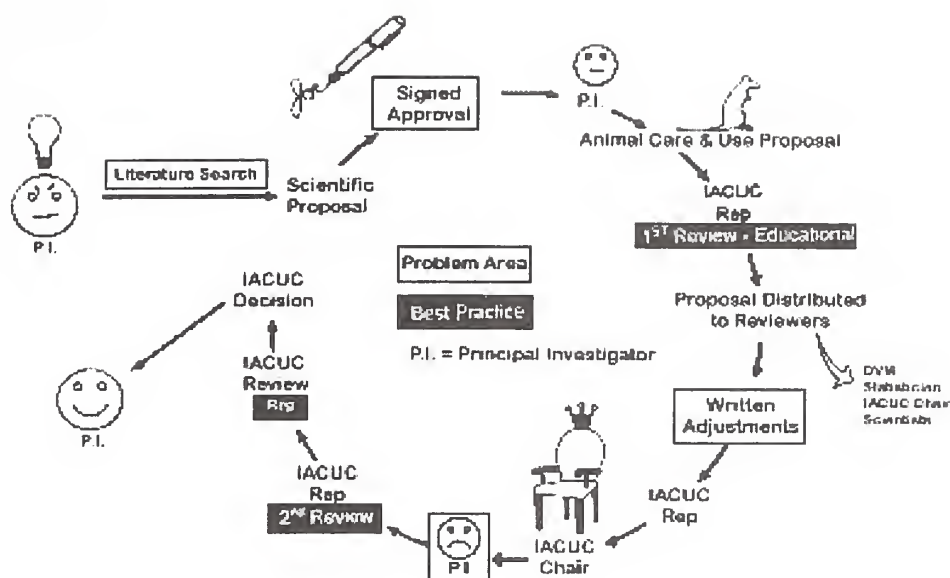


Figure 2. Pathway for successful scientific and animal care and use proposal review at the Armed Forces Radiobiology Research Institute

At AFRRI, the scientific review process is administratively separated from the IACUC review process. Thus, two documents—the scientific proposal and the animal use proposal—must be prepared. Unfortunately, an investigator may try to make parts of the scientific proposal also function as the animal care and use proposal by embedding scientific rationale and literature citations into the nontechnical explanation of the purpose in the animal use proposal and in the nontechnical description of the experimental design (**problem area**). This approach routinely causes IACUC community members to defer the proposal until only nontechnical language and selected references are used to describe the work. Furthermore, it provokes in-depth discussion that should be reserved for a specific scientific review.

At our institute, the scientific proposal must be approved by a hierarchy of scientific administrators. This arrangement, in addition to providing a review of the science, serves as a check on the duplication of effort relative to animal use (**best practice**). This process, however, takes time because the approval authorities are also involved in other administrative activities (**problem area**). Therefore, it is incumbent on all reviewers (especially those at the lowest supervisory level) to detect animal welfare issues that should be corrected before the animal use proposal is submitted for IACUC review.

## IACUC Review Process

Once the scientific proposal is approved the animal care and use proposal must be prepared. Before writing the animal care and use proposal, the investigator can benefit from informally reviewing the IACUC form with the departmental representative and the clinical veterinarian. Problem areas should be identified early to avoid extensive adjustments to the animal use proposal later.

When the investigator completes the IACUC form, it is submitted to the departmental representative for initial review. Since the representative may be familiar with the proposed research, input on fundamental scientific issues can be provided to the investigator in a diplomatic manner (2, 5). The review is provided as hardcopy, and the investigator adjusts the animal use proposal.

The investigator must realize that the animal use proposal is submitted into a process and is not evaluated against a static checklist of requirements. Each IACUC representative should also acquire the skill to teach an investigator about the animal welfare requirements as set forth in the IACUC form or ensure that the investigator knows where to find pertinent information.

The departmental representative submits the animal care and use proposal to the IACUC chairperson once he/she is satisfied with the investigator's adjustments in response to his/her comments. The IACUC chairperson, who evaluates all animal care and use proposals, distributes copies to a subcommittee composed of a clinical veterinarian, a statistician, two IACUC committee members acquainted with the subject species (5), and other IACUC members (7), if any, who wish to evaluate the proposal. So, including the departmental representative, the animal use proposal is reviewed by at least six different IACUC members.

Professionalism and respect for all parties during the animal care and use proposal review is maintained in the following way. Each IACUC subcommittee member evaluates the proposal and submits to the IACUC chairperson a written unsigned critique like that for a peer reviewed manuscript. Further, the IACUC chairperson inspects all critiques to ensure the fair and impartial application of animal welfare requirements. All unsigned critiques are then turned over to the investigator's IACUC representative who in turn releases all of them at one time to the investigator (**best practice**). If the investigator has serious concerns relative to fairness and impartiality of the critiques, he can appeal to the IACUC chairperson for adjudication and relief.

The failure to provide all critiques to the investigator at one time (**problem area**) can cause significant frustration. Although the IACUC reviewer may intend to save time for the investigator by providing an individual critique, the investigator could end up revising the proposal six times instead of once.

The review process described above is reasonably straightforward. Even so, proposals reviewed by the IACUC are often returned for additional information. When this happens, an investigator may view the IACUC and the IACUC chairperson as authoritarian (**problem area**), a critical situation that requires the utmost diplomacy and expert guidance on how to respond to the concerns documented in the critiques. It is important to explain to the investigator that specific scientific merit is not questioned and that the IACUC's concerns are with animal welfare and proper documentation (3) that satisfies all concerned parties indicated in figure 1.

Common reason for rejection of the animal care and use proposal is the lack of strong and thorough assurance documentation relative to duplication of research and alternatives for painful procedures. Investigators, in an effort to save time, may use the literature search used to establish the research proposal rationale (**problem area**). The IACUC must insist on a literature search that establishes whether pain can be alleviated or reduced and, if applicable, why less painful procedures cannot be used. As stated previously, valuable assistance in the performance of literature searches can be provided by the local librarian or the staff at AWIC.

The astute investigator responds to all the critiques and indicates in some manner to his/her IACUC departmental representative that all concerns of all IACUC reviewers were addressed. The departmental representative reviews the revised document (**best practice**) for compliance with adjustment requests and, if it is satisfactory, indicates to the IACUC chairperson that the animal care and use proposal is ready for full committee review. The animal care and use proposal is then placed on the IACUC agenda, which is distributed several days prior to the meeting.



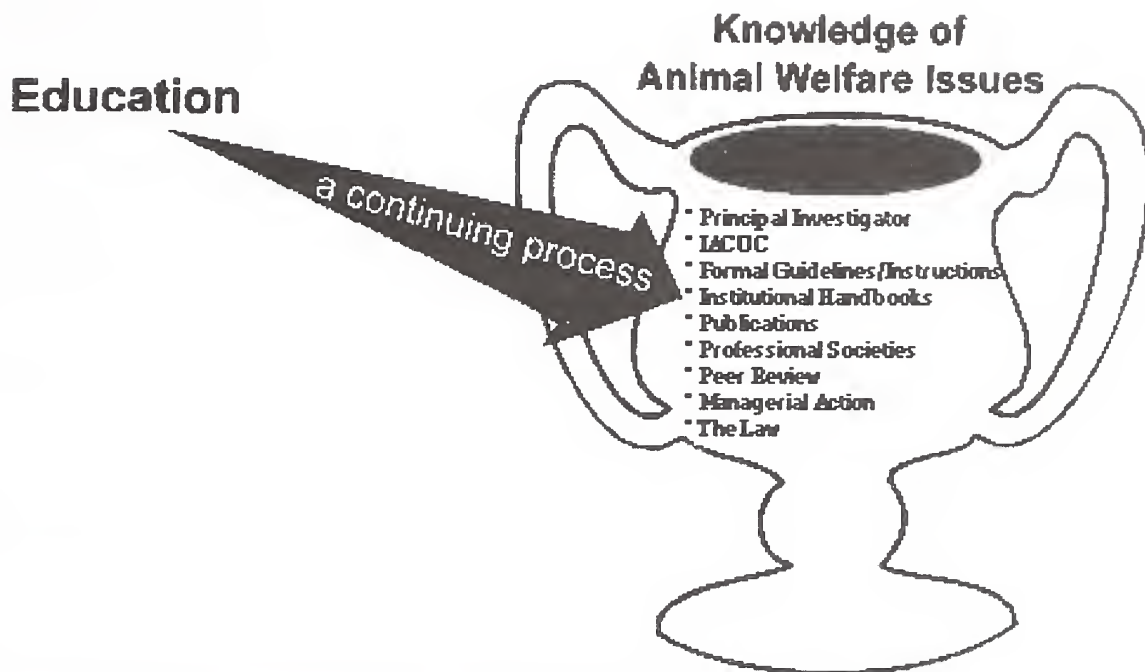


Figure 3. Sources of continuing education leading to knowledge in animal welfare issues.

The fully adjusted animal care and use proposal must meet with the approval of the departmental representative. At the meeting of the full IACUC membership, the chairperson again offers to all IACUC members the opportunity to review the adjusted animal use proposal. If there are no requests, the departmental representative (**best practice**) provides an oral review of the proposal and stands for questions from the whole committee. The investigator may be invited and may request to present the review. If not presenting the review, the investigator is alerted to be in the vicinity of the meeting area to answer technically difficult questions. Based on the relationship that develops during the review process, most investigators trust their departmental representative to present the review. Likewise, many investigators are uncomfortable or even intimidated by a committee of their peers who reviewed their work.

• When all concerns have been addressed by the investigator, the animal care and use proposal is brought to a vote. If present, the investigator and anyone with a vested interest is invited to leave the room. Voting by secret ballot or by voice is offered. An "approved" decision is justified if all parties have been attentive to the IACUC role of oversight of the animal welfare rules and regulations. If the proposal is approved, the decision is documented in the meeting minutes, the proposal is stamped, signed, and dated by the IACUC chairperson, the investigator is notified, and the original document is kept in the permanent IACUC files. If disapproved, the proposal is returned to the investigator via the IACUC representative for additional information or revision.

## Conclusion

The Animal Welfare Act mandates that the IACUC is the formal overseer of animal welfare in the local research environment. However, this does not release any participant from ensuring that animals are humanely used and that integrity (1) is central to all research and testing endeavors. Education relative to animal welfare, inside and outside of the IACUC, is a continuing process (fig. 3). Enlightened staff realize that there are many avenues to this knowledge and that, once achieved, produces better research products.



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# Federal Criteria for Granting IACUC Approval

(From the ARENA/NIH IACUC Guidebook)

<b>Activities</b>	Must be in accord with USDA Regulations/PHS Policy.
<b>Pain/Distress</b>	Must avoid/minimize discomfort, distress, and/or pain. If pain/distress is caused, appropriate sedation, analgesia or anesthesia will be used. Attending veterinarian must be involved in planning. Use of paralytics without anesthesia is prohibited. Animals with chronic/severe unrelievable pain will be painlessly killed.
<b>Surgery</b>	Must meet requirements for sterile surgery and pre/postoperative care. Cannot use one animal for several major operative procedures from which it will recover, without meeting specified conditions.
<b>Euthanasia</b>	Euthanasia method must be consistent with USDA Regulations/AVMA recommendations.
<b>Housing/Health</b>	Animal living conditions must be consistent with standards of housing, feeding and care directed by veterinarian or scientist with appropriate expertise.
<b>Alternatives</b>	There must be considered alternatives to painful procedures; also must document consideration of alternatives if animals experience pain or suffering.
<b>Rationale and Methods</b>	Must provide written narrative of methods/sources.
<b>Duplication</b>	Must provide assurance that activities do not unnecessarily duplicate previous efforts.
<b>Qualifications</b>	Personnel must be appropriately qualified.
<b>Deviations from Requirements</b>	Must be justified for scientific reasons, in writing.



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NAL call number: QL55.N48  
Descriptors: ACUC, animal review committee, expedited process, full committee review.

## Protocol Review

This is a regular column in the magazine *Lab Animal*. The column coordinator is Jerald Silverman, DVM, who describes a hypothetical IACUC scenario and has members of the research community resolve the issue. Below is a partial list of column references.

NAL call number: QL55 A1L33

**Going fishing.** (1999) 28(4): 16-17.

Descriptors: questionable hypothesis unsupported by scientific literature, unpublished data, toxicology protocol previously approved for other compounds, scientific validity for testing compounds received under contract.

**The moral balance.** (1999). 28(3):

Descriptors: pain, neonatal animals, use of 1 rabbit kit per litter from 75 animals, disposition of remaining animals, options available to the IACUC.

**To have and to hold.** (1999). 28(2):

Descriptors: animals with unique genotype, completed research project, conflict between grantee IACUC and IACUC at facility where research was conducted over authorization to transfer animals to another institution, adoption, payment of shipping costs, PHS, animal protocol form, investigator-IACUC communication, establishment of ownership.

**Proprietary paranoia.** (1999) 28(1): 18-19.

Descriptors: proprietary information, confidentiality, toxicology of pharmaceuticals, humane endpoints.

**So much work, so little time.**(1998) 27(8): 16-18.

Descriptors: workflow, communication, voting, role of the IACUC chair, OPRR and USDA commentary provided.

**Playing by the rules.** (1998) 27(3): 19-21.

Descriptors: post operative analgesics, Animal Welfare Act interpretation, interference with proposed methods.

**Don't bug me.** (1998) 27(2): 19-20.

Descriptors: funding, parasites due to animal transport within the facility, limited space for animal care.

**Power struggle.** (1997) 27(1): 22-23.

Descriptors: communication, authority over animal care, standard operating procedures.

**Long Distance IACUC.** (1997) 26(10): 22-24.

Descriptors: electronic meetings, email, conference calls.

**By the book?** (1997) 26(9): 23-25.

Descriptors: pain perception, *Xenopus*, multiple survival surgeries.

**Much ado about nothing?** (1997) 26(8): 24-26.

Descriptors: pain, analgesics confound research results, acupuncture.

**Form follows function.** (1997) 26(7): 22-24.

Descriptors: continuity of a protocol when transferring from one institution to another, new review.

**Someone squealed.** (1997) 26(6): 20-22.

Descriptors: whistleblowing, confidentiality, subcommittee.

**Triangulating company politics.** (1997) 26(5): 19-22.

Descriptors: authority conflicts, public-private collaborations.

**Attempted pig embezzlement.** (1997) 26(4): 18-20.

Descriptors: animal housing at home, investigator-IACUC disagreements.

**Optimal animal use.** (1997) 26(3): 20-22.

Descriptors: dead animals, shared tissues, redundant protocols, USDA and PHS responses.

**Choose wisely.** (1997) 26(2): 19-20.

Descriptors: choosing a non-affiliated member, community representation, criteria.

**An information specialist's domain.** (1997) 26(1): 20-21.

Descriptors: databases, alternatives searches, search strategies, usefulness.

**Pilot to IACUC.** (1996) 25(10): 21-22.

Descriptors: justifying animal numbers, pilot studies.

**Adaptation or distress.** (1996) 25(9): 21-22.

Descriptors: identification of distress, disease studies, adaptation to disease, unalleviated distress.

**Majority rules.** (1996) 25(8): 21-22.

Descriptors: quorum, full committee, voting, USDA and PHS responses.

**Pentobarbital and the Cheshire cat.** (1996) 25(7): 22-25.

Descriptors: anesthesia methods, professional guidelines and accepted practices, personal experience.

**Pig hearts and dog models.** (1996) 25(6): 21-22.

Descriptors: choice of animal models, validating and justifying new models.

**A chicken and egg situation.** (1996) 25(5): 20-23.

Descriptors: nonvertebrate embryos become vertebrate hatchlings, policy development, planning.

**Socrates meets the Great Eastern University.** (1996) 25(4): 22-23.

Descriptors: justification of research, scientific merit, open meetings.

**An IACUC confounded.** (1996) 25(3): 24-26.

Descriptors: vaccine testing, alternatives, Food and Drug Administration, primate requirements.

**Playing favorites.** (1996) 25(2): 20-21.

Descriptors: multiple major survival surgeries, technician concern, animal welfare.

**Problem child.** (1996) 25(1): 19-20.

Descriptors: multiple minor animal care and use problems with a single principal investigator over time, case considerations, constructive approaches.

**Does a fetus feel pain?** (1995) 24 (9): 21-22.

Descriptors: rats, fetus, pain, animal welfare, animal experiments.

**A researcher's quagmire.** (1995) 24(5): 24-25.

Descriptors: survival surgery, refinement, reporting, multiple surgeries.

**Subcontractor or merchant?** (1994) 23(7): 21-22.

Descriptors: animal transfer to contractors, oversight, PHS assurance, ownership.

**Curbing drug abuse.** (1989) 18(5): 23.

Descriptors: drug use, rodents, drug effects, ACUC.

**Survival surgical procedures.** (1988) 16(6): 25-26.

Descriptors: personnel requirements, facilities, aseptic surgical procedures.

**Surgical suite alternative.** (1989) 18(7): 22.

Descriptors: surgical procedures, guinea pigs, laboratory operating area.

**Project reassessment.** (1987) 16(2): 23-24.

Descriptors: rabbits, hemorrhage, projects, ACUC.

**Limb regeneration in mammals.** (1988) 17(5): 22-23.

Descriptors: rats, limbs, amputation, wound healing.

**Unattended animals.** (1989) 18(1): 15.

Descriptors: rat, investigator responsibilities.

**Experimental hypothermia.** (1989) 18(3): 18.

Descriptors: rats, submersion, animal distress.

Rowan, A.N. (1990). **Ethical review and the animal care and use committee.** *Hastings Center Report* 20(3 Supp.): 19-24.

NAL call number: R724 H27

Descriptors: Laboratory Animal Welfare Act of 1966, social aspects, Animal Welfare Act of 1970, ethics, animal experimentation, research institutes, standards.

Russow, L-M. (1995). **Protocol Review: Too much paperwork?** In *"Current Issues and New Frontiers in Animal Research*, K.A.L. Bayne, M. Greene, and E.D. Prentice, eds., Greenbelt, Maryland: Scientists Center for Animal Welfare, pp. 15-18.

NAL call number: HV4913 C87 1995

Descriptors: information required by IACUC, development of protocol forms, ethics, roles of IACUC members.

Stafleu, F.R., B.D. Baarda, F.R. Heeger, and A.C. Beynen (1993). **The influence of animal discomfort, human interest and scientific quality on the ethical acceptability of a projected animal experiment as assessed with questionnaires.** *Alternatives to laboratory animals: ATLA* 21 (2): 129-137.

NAL call number: Z7994.L3A5.



AB- This study attempts to assess to what extent three selected variables (animal discomfort, scientific quality and human interest) determine the ethical acceptability of a projected animal experiment, as judged by animal experimenters. Two levels of each of the three variables were incorporated into otherwise identical protocols of a hypothetical animal experiment. Thus, there were eight different protocols with various combinations of the variables. In a postal survey, animal experimenters were asked to assign an acceptability score to the projected animal experiment described and to give a short written justification of their score. Human interest had the greatest influence on acceptability scores, followed by animal discomfort and scientific quality. Arguments concerning scientific quality played a major role in determining acceptability scores. At high levels of animal discomfort, the projected experiment was considered acceptable when both human interest and scientific quality were high. Thus, it remains questionable whether, in practice, a well-designed experiment with significant, expected human interest would be dismissed because of a high or moderate degree of anticipated animal discomfort.

Descriptors: animal experiments, animal welfare, bioethics.

Staflue, F.R., B.D. Baarda, F.R. Heeger, and A.C. Beynen (1994). **The influence of animal discomfort and human interest on the ethical acceptability of projected animal experiments.** In *Welfare and science: proceedings of the Fifth Symposium of the Federation of European Laboratory Animal Science Associations, 8-11 June 1993*, Brighton, London: Royal Society of Medicine Press, pp. 278-280.

NAL call number: QL55.F43 1993.

Descriptors: laboratory animals, animal experiments, ethics, pain, animal welfare, questionnaires, man, health protection.

Steneck, N.H. (1997). **Role of the institutional animal care and use committee in monitoring research.** *Ethics Behavior* 7(2): 173-184.

Descriptors: animal care, ethics, committees, regulation, .

Tomson, F.N. (1989). **Approving the use of animals in medical education.** *Theoretical Medicine* 10(1): 35-42.

Descriptors: animal welfare, laboratory animals, standards, attitude of health personnel.

## Useful World Wide Web Sites

### Protocol Review Procedures

<http://www.ra.utk.edu/ora/labanim1/UTBYLAW6.html>

This site is provided by the University of Tennessee at Knoxville Institutional Animal Care and Use Committee. Click on protocol review procedures.

### Review of Protocols, National Institutes of Health, Office for Protection from Research Risks

<http://grants.nih.gov/grants/oprr/pubartindex.htm#i>

The following articles can be viewed from this site:

- Annual review (USDA) vs. triennial review (PHS)  
ILAR News. 1991; 33(4):68-70, question #8.
- Authority of IACUC  
Lab Animal. 1997;26(3):21.
- Expedited review  
ILAR News. 1993; 35(3-4):47-49, question #3.  
OPRR Reports. 1990; 90-01, 5/21/90.

- Frequency of review  
ILAR News. 1993; 35(3-4):47-49, question #7.
- Model for performing continuing review of research activities  
Contemporary Topics. 1996; 35(5):53-56.
- Process for review  
Lab Animal. 1998:27(8):18.
- Review of grant applications  
Lab Animal. 1999:28(7):21.
- Scientific merit review  
ILAR News. 1991; 33(4):68-70, question #7.
- Significant changes to approved protocols  
Lab Animal. 1995; 24(9):24-26, question #1.
- Tracking the number of animals used  
Contemporary Topics. 1997; 36(2):47-50, question #7.
- Use of cold-blooded vertebrates  
Contemporary Topics. 1997; 36(2):47-50, question #6.



# Attending Veterinarian







# Attending Veterinarian and Adequate Veterinary Care

9 CFR, Subchapter A, Animal Welfare, §2.32

This document is available at <http://www.access.gpo.gov/nara/cfr/waisidx/9cfr2.html>

(a) Each research facility shall have an attending veterinarian who shall provide adequate veterinary care to its animals in compliance with this section:

(1) Each research facility shall employ an attending veterinarian under formal arrangements. In the case of a part-time attending veterinarian or consultant arrangements, the formal arrangements shall include a written program of veterinary care and regularly scheduled visits to the research facility;

(2) Each research facility shall assure that the attending veterinarian has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use; and

(3) The attending veterinarian shall be a voting member of the IACUC; Provided, however, That a research facility with more than one Doctor of Veterinary Medicine (DVM) may appoint to the IACUC another DVM with delegated program responsibility for activities involving animals at the research facility.

(b) Each research facility shall establish and maintain programs of adequate veterinary care that include:

(1) The availability of appropriate facilities, personnel, equipment, and services to comply with the provisions of this subchapter;

(2) The use of appropriate methods to prevent, control, diagnose, and treat diseases and injuries, and the availability of emergency, weekend, and holiday care;

(3) Daily observation of all animals to assess their health and well-being; Provided, however, That daily observation of animals may be accomplished by someone other than the attending veterinarian; and Provided, further, That a mechanism of direct and frequent communication is required so that timely and accurate information on problems of animal health, behavior, and well-being is conveyed to the attending veterinarian;

(4) Guidance to principal investigators and other personnel involved in the care and use of animals regarding handling, immobilization, anesthesia, analgesia, tranquilization, and euthanasia; and

(5) Adequate pre-procedural and post-procedural care in accordance with current established veterinary medical and nursing procedures.

# Ensuring Adequate Veterinary Care: Roles and Responsibilities of Facility Owners and Attending Veterinarians

March 1999

USDA, APHIS, Animal Care

<http://www.aphis.usda.gov/oa/pubs/tneavc.html>

Under the Animal Welfare Act, the U.S. Department of Agriculture's (USDA) Animal and Plant Health Inspection Service (APHIS) requires that all persons who use animals in research or for exhibition, sell them at the wholesale level, or transport them in commerce provide these animals with adequate veterinary care and animal husbandry. Toward this end, APHIS requires the owner of each licensed and registered facility to establish a formal program of veterinary care. Facility owners must also employ an attending veterinarian to oversee the care afforded the animals.

## Essential Components of a Veterinary Care Program

APHIS personnel assess each facility's veterinary care program to determine whether it contains the following elements:

- ★ Appropriate facilities, personnel, equipment, and services to provide adequate veterinary care.
- ★ Use of appropriate methods to prevent, control, diagnose, and treat diseases and injuries.
- ★ Availability of emergency, weekend, and holiday care for animals.
- ★ Daily observation of all animals by employees to assess the animals' health and well-being.
- ★ Direct and frequent communication between the facility and attending veterinarian on any veterinary care concerns.
- ★ Adequate guidance and training of personnel who care for animals regarding handling, immobilization, anesthesia, analgesia, tranquilization, and euthanasia.
- ★ Provisions for adequate preprocedural and postprocedural care in accordance with established veterinary medical and nursing procedures.

## The Role of the Attending Veterinarian

The attending veterinarian is responsible for reviewing the facility's veterinary care program at least once a year. Facilities must employ their veterinarians under the following terms:

- ★ The facility must employ its veterinarian under formal arrangements on a full-time, part-time, or consulting basis. The facility owner must be able to prove employment of the veterinarian, either through a contract or other written documentation.
- ★ If the veterinarian is part-time or consulting, the facility owner must prepare a written program of veterinary care. The owner must also schedule regular visits by the attending veterinarian at least once a year. The facility owner is solely responsible for scheduling these visits.
- ★ The facility owner must give the veterinarian sufficient authority to ensure adequate veterinary care for the animals.

## Specifics to Check For During a Veterinary Care Program Review

When conducting a review of a facility's veterinary care program, the attending veterinarian should check for vaccinations, parasite-control programs, euthanasia methods, exercise programs for

dogs, environmental enrichment programs for primates, and several other specific provisions. The checklist on this tech note provides a detailed list of these provisions for use in evaluating specific veterinary care programs. (See Veterinary Care Checklist following this article)

### **Additional Information**

For more information, or if you have other questions about the veterinary care requirements under the Animal Welfare Act, contact your local APHIS Animal Care inspector or field veterinary medical officer, or:

Animal Care  
APHIS, USDA  
Unit 84  
4700 River Road  
Riverdale, MD 20737  
Telephone: (301) 734-7833  
E-mail: [ace@usda.gov](mailto:ace@usda.gov)  
Web page: <http://www.aphis.usda.gov/ac>



# Veterinary Care Checklist

This checklist should be used when reviewing a facility's veterinary care program and kept on file at the facility for review by APHIS personnel.

Facility Name: \_\_\_\_\_

Date of Visit: \_\_\_\_\_

Review each item below with the facility owner. Place an "x" next to each item discussed and "N/A" next to those items that are not applicable.

- \_\_\_\_ Vaccinations
- \_\_\_\_ Parasite control program
- \_\_\_\_ Emergency care
- \_\_\_\_ Euthanasia methods
- \_\_\_\_ Nutritive value of diets
- \_\_\_\_ Handling of biologics and drugs
- \_\_\_\_ Pest control and product safety
- \_\_\_\_ Quarantine procedures
- \_\_\_\_ Exercise program (dogs only)
- \_\_\_\_ Environmental enrichment (primates only)
- \_\_\_\_ Water quality (marine mammals only)
- \_\_\_\_ Capture and restraint methods (wild or exotic animals only)
- \_\_\_\_ General observations
- \_\_\_\_ overall facility condition
- \_\_\_\_ general animal husbandry practices

Comments and recommendations on overall health of animals and effectiveness of veterinary care program:

Signature of Attending Veterinarian:

# Veterinary Medical Care

Excerpted from the *Guide to the Care and Use of Laboratory Animals*, p. 56.

Veterinary medical care is an essential part of an animal care and use program. Adequate veterinary care consists of effective programs for:

- Preventive medicine.

- Surveillance, diagnosis, treatment, and control of disease, including zoonosis control.

- Management of protocol-associated disease, disability, or other sequelae.

- Anesthesia and analgesia.

- Surgery and postsurgical care.

- Assessment of animal well-being.

- Euthanasia.

A veterinary-care program is the responsibility of the attending veterinarian, who is certified or has training or experience in laboratory animal science and medicine or in the care of the species being used. Some aspects of the veterinary-care program can be conducted by persons other than a veterinarian, but a mechanism for direct and frequent communication should be established to ensure that timely and accurate information is conveyed to the veterinarian on problems associated with animal health, behavior, and well-being. The veterinarian must provide guidance to investigators and all personnel involved in the care and use of animals to ensure appropriate handling, immobilization, sedation, analgesia, anesthesia, and euthanasia. The attending veterinarian must provide guidance or oversight to surgery programs and oversight of postsurgical care.

# Adequate Veterinary Care

## Public Position Statement of The American College of Laboratory Animal Medicine

This document is available at [http://www.aclam.org/aclam/adeqvet.htm#adequate care](http://www.aclam.org/aclam/adeqvet.htm#adequate%20care)

### I. Introduction

These guidelines were prepared by the American College of Laboratory Animal Medicine (ACLAM) to assist in the formulation and evaluation of programs of veterinary care for laboratory animals. The professional judgement of a trained and experienced veterinarian is essential in the application of these guidelines to specific institutional settings.

The ACLAM recognizes that both regulatory and science sponsoring agencies such as the United States Department of Agriculture (USDA) and the Public Health Service of the United States Department of Health and Human Services (PHS/DHHS), through their respective regulations and policies, support the concept of "adequate veterinary care" within their own range of interest and specialization. This document, written by ACLAM, an organization comprised of veterinarians certified in the specialty of laboratory animal medicine, is a detailed description of adequate veterinary care and is intended to apply to animals used, or intended for use, in research, teaching or testing.

### II. ACLAM Position On Adequate Veterinary Care

The institutional veterinarian must be qualified by virtue of appropriate postgraduate training or experience in laboratory animal science and medicine. Such training and experience are indicated by certification by ACLAM and/or participation in laboratory animal medicine continuing education activities of ACLAM and the American Society of Laboratory Animal Practitioners. The continuing education of the veterinarian is an essential component of maintaining competence.

The extent of the veterinary care program will depend on several factors, such as: (1) the number of animals, (2) the species used and (3) the nature of the experimentation conducted. Large units may need several veterinarians to fulfill the program's requirements. One veterinarian may be sufficient in moderately sized units, and a part-time or consulting veterinarian may be acceptable in small units.

However, in all cases, formal arrangements for the provision of veterinary care must be made. Consulting veterinarians must make regularly scheduled visits (frequency based on need), and arrangements must be made to assure that veterinary services are readily available at all other times to meet either routine or emergency needs.

The veterinarian responsible for supporting an institutional animal care and use program must have appropriate authority to execute the duties inherent in assuring the adequacy of veterinary care and overseeing other aspects of animal care and use to ensure that the program meets applicable standards. The veterinarian must be fully knowledgeable concerning the current and proposed use of animals in the institutional research, testing and teaching programs.

At least one veterinarian must be a full member of the Institutional Animal Care and Use Committee (IACUC) and actively involved in the review of all protocols and projects, and in the inspection of facilities and review of institutional programs involving animals in research, testing and teaching. For the veterinary care program to be judged "adequate", there is a continuing institutional responsibility to foster and support enhancement of the program through the identification and adoption of techniques, procedures and policies that improve laboratory animal health and well-being.

ACLAM endorses the American Veterinary Medical Association Principles of Veterinary Ethics and the specific guidelines regarding veterinarians employed by other than veterinary medical organizations. Veterinarians must be especially vigilant in ensuring that their professional veterinary judgments are neither influenced nor controlled by institutional interests to the detriment of the laboratory animals.

The provision of adequate veterinary care involves the following primary areas of responsibility:

#### **A. Disease Detection and Surveillance, Prevention, Diagnosis, Treatment and Resolution**

1. The isolation, quarantine and stabilization programs for newly arrived animals are necessary to provide time to assess their health status, allow them to recover from the stress of shipment and an opportunity to adapt to their new environment. The extent of these programs depends on several factors, including species and source of the animals as well as their intended use. For some animals, such as rodents obtained from reliable sources for which health status is known, visual inspection on arrival may suffice. For species such as nonhuman primates, farm animals, wild animals, random source dogs and cats, and non-specific pathogen free rabbits and rodents, appropriate quarantine and isolation procedures must be employed.

2. Preventive medicine programs such as vaccinations, ecto- and endoparasite treatments and other disease control measures should be initiated according to currently acceptable veterinary medical practices appropriate to the particular species and source. Only animals of defined health status should be used in research and testing unless a specific, naturally occurring or induced disease state is being studied. Systems should be established to protect animals within the institution from exposure to diseases. Transgenic and mutant animals may be particularly susceptible to diseases and may require special protection to ensure their health. Systems to prevent spread of disease may include facility design features, containment/isolation equipment, and use of standard operating procedures. Training of animal care and research staff is essential to prevent spread of animal diseases.

3. Daily observation of all animals by a person or persons qualified to verify their well-being is required. It is not necessary for a veterinarian to personally make this assessment each day. However, at a minimum, a trained paraprofessional or technician must observe each animal every day and there must be a timely and accurate method for conveying information regarding animal health, behavior and well-being to the veterinarian.

4. Disease surveillance is a major responsibility of the veterinarian and should include routine monitoring of colony animals for the presence of parasitic, bacterial and viral agents that may cause overt or inapparent disease. Additionally, cells, tissues, fluids, and transplantable tumors that are to be used in animals should be monitored for infectious or parasitic agents that may cause disease in animals. The type and intensity of monitoring necessary will depend upon professional veterinary judgement and the species, source, use and number of animals housed and used in the facility.

5. Diagnostic laboratory services must be available and used as appropriate. Laboratory services should include necropsy, histopathology, microbiology, clinical pathology, serology, and parasitology as well as other routine or specialized laboratory procedures, as needed. It is not necessary that all of these services be available within the animal facility if other laboratories with appropriate capabilities are available and used.

6. Animals with infectious disease must be isolated from others by placing them in isolation units or separate rooms appropriate for the containment of the agents of concern. In certain circumstances, when an entire group of animals is known or thought to be exposed or infected, it may be appropriate to keep the group intact during the time necessary for diagnosis and treatment, for taking other control measures, or for completion of a project.



7. The veterinarian must have authority to use appropriate treatment or control measures, including euthanasia if indicated, following diagnosis of an animal disease or injury. If possible, the veterinarian should discuss the situation with the principal investigator to determine a course of action consistent with experimental goals. However, if the principal investigator is not available, or if agreement cannot be reached, the veterinarian must have authority to act to protect the health and well-being of the institutional animal colony. The veterinarian's authority should be exercised with the concurrence of the IACUC and the Institutional Official.

## **B. Handling and Restraint; Anesthetics, Analgesics and Tranquilizer Drugs; and Methods of Euthanasia**

Adequate veterinary care includes providing guidance to animal users and monitoring animal use to assure that appropriate methods of handling and restraint are being used and to ensure proper use of anesthetics, analgesics, tranquilizers, and methods of euthanasia. Written guidelines regarding the selection and use of anesthetics, analgesics and tranquilizing drugs and euthanasia practices for all species used must be provided and periodically reviewed by the veterinarian. Guidelines may be developed in-house or provided by specific references to the current veterinary literature. In addition, the veterinarian or trained paraprofessionals should provide formal or informal instruction in the proper use of such agents and euthanasia procedures.

The veterinarian must have the responsibility and authority to assure that handling, restraint, anesthesia, analgesia and euthanasia are administered as required to relieve pain and such suffering in research animals, provided such intervention is not specifically precluded in protocols reviewed and approved by the IACUC. The veterinarian must exercise good professional judgement to select the most appropriate pharmacologic agent(s) and methods to relieve animal pain or distress in order to assure humane treatment of animals, while avoiding undue interference with goals of the experiment.

## **C. Surgical and Postsurgical Care**

A program of adequate veterinary care includes the review and approval of all preoperative, surgical and postoperative procedures by a qualified veterinarian. The institution bears responsibility and must assure, through authority explicitly delegated to the veterinarian or to the IACUC, that only facilities with programs appropriate for the intended surgical procedures are utilized and that personnel are adequately trained and competent to perform the procedures. The veterinarian's inherent responsibility includes monitoring and providing recommendations concerning preoperative procedures, surgical techniques, the qualifications of institutional staff to perform surgery and the provision of postoperative care.

## **D. Animal Well-Being**

Adequate veterinary care includes responsibility for the promotion and monitoring of an animal's well-being before, during and after experimentation or testing. Animal well-being includes both physical and psychological aspects of an animal's condition evaluated in terms of environmental comfort, freedom from pain and distress and appropriate social interactions, both with conspecifics and with man. The veterinarian must have the authority and responsibility for making determinations concerning animal well-being and assuring that animal well-being is adequately monitored and promoted. The veterinarian must exercise this responsibility in review of animal care and use protocols, and must have the authority to remove an animal from an experiment which is adversely affecting its well-being beyond a level reviewed and approved by the IACUC.

The following examples represent how this responsibility can be met:

Ensuring the adequacy of the physical plant, caging and ancillary equipment.

Developing, implementing and monitoring sound animal care (husbandry) programs including such areas as sanitation, nutrition, genetics and breeding and vermin control.

Establishing an acclimatization program to adapt animals to either short-term or long term restraint procedures.

Improving and enriching an animal's environment to minimize the development of physical or behavioral abnormalities.

Providing appropriate opportunities for human-animal socialization and acclimatization to the research environment or procedures.

Performing periodic physical and clinical evaluations appropriate for the species and the experimental situation.

Providing pre-procedural and post-procedural care in accordance with current established veterinary procedures.

### **E. Appropriate Use of Animals in Research and Testing**

The veterinarian must be involved in the review and approval of all animal care and use in the institutional program. This includes advising on the design and performance of experiments using animals as related to model selection, collection and analysis of samples and data from animals, and methods and techniques proposed or in use. This responsibility is usually shared with investigators, the IACUC, and external peer reviewers.

### **III. Related Concerns**

Other areas of professional concern and responsibility for the veterinarian which may not strictly be part of the ACLAM description of adequate veterinary care include the following:

Participating in the development and administration of training for institutional staff in the care and use of laboratory animals.

Assisting institutional health officials to establish and monitor an occupational health program for all animal care workers and others who have substantial animal contact.

Monitoring for zoonotic diseases such as leptospirosis, toxoplasmosis, rabies, Q-fever, B-virus infection, hantavirus infection, and lymphocytic choriomeningitis.

Advising on and monitoring of standards of hygiene among institutional staff involved with research animal care and use.

Advising on and monitoring of biohazard control policies and procedures as they apply to research animal care and use.

### **IV. Conclusions**

The Diplomates of the American College of Laboratory Animal Medicine believe that adequate veterinary care is an integral component of humane animal care and use in research, teaching and testing and further, that the state of animal well-being ensured through adequate veterinary care is essential to reliability of results from experimentation with animals. The essential components of adequate veterinary care programs for laboratory animals include: a) one or more qualified veterinarians and veterinary technical staff, b) authority to implement the veterinary care program and provide oversight of related aspects of the institutional animal care and use program, c) disease

prevention, diagnosis and control programs, d) guidance for research staff in animal methods and techniques, and e) the promotion of animal well-being.

# Attending Veterinarian Bibliography

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NAL call number: QL55.A1L33.  
Descriptors: veterinarians, committees.
- Fisk, S.K. (1978). **Don't overlook the lab animal veterinarian.** *Lab Animal* 7(2): 37.  
NAL call number: QL55 A1L33  
AB- What this professional can contribute to research projects.
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Descriptors: veterinarians, professional ethics, animal diseases, animal welfare, theft.
- Pakes, S.P. (1990). **Contributions of the laboratory animal veterinarian to refining animal experiments in toxicology.** *Fundamentals of Applied Toxicology* 15(1): 17-24.  
Descriptors: animal pain, psychology, measurement, research design, alternatives, trends, veterinarians, ACUC.
- Quimby, F.W. (1995). **The role of attending veterinarians in laboratory animal welfare.** *Journal of the American Veterinary Medical Association* 206(4): 461-5.  
Descriptors: Animal Welfare Act, legislation, ethics, United States Department of Agriculture.
- Scott, L.R. and P.D. Carter. (1996). **The role of veterinarians on animal experimentation ethics committees.** *Australian Veterinary Journal* 74 (4): 309-311.  
NAL call number: 41.8 Au72  
Descriptors: animal experiments, animal welfare, veterinarians, bioethics, committees, organizations.
- Stark, D.M. (1989). **The American veterinarians' role and education in laboratory animal science.** *Animal Technology: Journal of the Institute of Animal Technicians* 40(3): 199-201.  
NAL call number: QL55 I5  
Descriptors: laboratory animals, training, animal husbandry, ACUC.
- Van Hoosier, Jr, G.L. (1987). **Role of the veterinarian.** *Laboratory Animal Science* 37(special issue): 101-102.  
NAL call number: 410.9 P94  
Descriptors: laboratory animals, animal welfare, ACUC.

## Useful World Wide Web Sites

### University of Arizona Institutional Animal Care and Use Committee, Authority of the Attending Veterinarian

<http://www.ahsc.arizona.edu/uac/iacuc/special.shtml#vet>

An example of a short, concise policy.

### University of California at Irvine, Veterinary Consultations

<http://www.rgs.uci.edu/rig/asvetcon.htm>

Topics covered include: issues related to protocol preparation, scope of veterinary care, what kind of animals to use.



**University of Kansas-Lawrence, Responsibilities of the Animal Care Unit**

<http://www.ukans.edu/~acu/chapter1.html>

This site lists various institutional policies and regulations.

**University of Tennessee at Knoxville, Attending Veterinarian/Researcher Veterinarian**

<http://www.ra.utk.edu/ora/labaniml/ATTENVET.html>

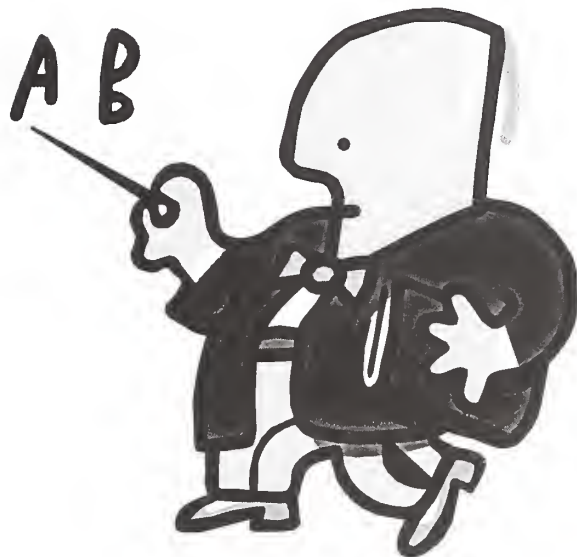
The purpose of this statement is to distinguish between the attending veterinarian and the veterinarian who is also a researcher and their respective responsibilities.

**Veterinarians In Research Labs Address Conflicting Agendas**

[http://165.123.33.33/yr1997/may/finn\\_p1\\_970526.html](http://165.123.33.33/yr1997/may/finn_p1_970526.html)

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# Training





# When the USDA Veterinary Medical Officer Looks at Your Training Program

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This paper was originally presented at the 1998 Laboratory Animal Welfare Training Exchange conference held in St. Louis, Missouri.

The Animal Welfare Act mandates that each research facility shall provide for the training of scientists, animal technicians, and other personnel involved with animal care and treatment in the facility.

Title 9 - Code of Federal Regulations - Chapter 1, Subchapter A - Animal Welfare §2.32 gives specific requirements for training as follows:

- (a) It shall be the responsibility of the research facility to ensure that all scientists, research technicians, animal technicians, and other personnel involved in animal care, treatment, and use are qualified to perform their duties. This responsibility shall be fulfilled in part through the provision of training and instruction to those personnel.
- (b) Training and instruction shall be made available, and qualifications of personnel reviewed, with sufficient frequency to fulfill the research facility's responsibilities under this section and §2.31.
- (c) Training and instruction of personnel must include guidance in at least the following areas:
  - (1) Humane methods of animal maintenance and experimentation, including:
    - (i) The basic needs of each species of animal;
    - (ii) Proper handling and care for the various species of animals used by the facility.
    - (iii) Proper pre-procedural and post-procedural care of animals; and
    - (iv) Aseptic surgical methods and procedures.
  - (2) The concept, availability, and use of research or testing methods that limit the use of animals or minimize animal distress.
  - (3) Proper use of anesthetics, analgesics, and tranquilizers for any species of animals used by the facility.
  - (4) Methods whereby deficiencies in animal care and treatment are reported, including deficiencies in animal care and treatment reported by any employee of the facility. No facility employee, committee member, or laboratory personnel shall be discriminated against or be subject to any reprisal for reporting violations of any regulation or standards under the Act,
  - (5) Utilization of Services (e.g., National Agricultural Library, National Library of Medicine) available to provide information;
    - (i) On appropriate methods of animal care and use;
    - (ii) On alternatives to the use of live animals in research;
    - (iii) That could prevent unintended and unnecessary duplication of research involving animals; and
    - (iv) Regarding the intent and regulation of the Act.

The IACUC of each research facility is charged with the responsibility of reviewing on a semi-annual basis the research facility's entire program for humane care and use of animals. A vital



component of every program is the training of all personnel involved in animal care, treatment, and use.

The IACUC must determine that all personnel conducting procedures on animals being maintained or studied are appropriately qualified and trained in those procedures.

The USDA veterinary medical officer, when inspecting a research facility, has the challenging task of evaluating the facility's overall training program.

This evaluation process should involve asking the following questions:

- ★ Is training and instruction available to all personnel involved in animal care, treatment, and use?
- ★ Does the training program include guidance in all areas listed in §2.32 - Personnel qualifications of the regulations?
- ★ Is there adequate documentation of qualifications and training of personnel?
- ★ Has the IACUC been provided sufficient documentation for it to fulfill its tasks of reviewing qualifications and training of all personnel involved in all proposed or ongoing activities?
- ★ Does the semi-annual program review of animal care and use include personnel qualifications and training?
- ★ Has there been input and oversight by the attending veterinarian toward an effective training program?
- ★ Are procedures being adequately monitored to insure competency in situations such as new or inexperienced personnel?
- ★ How does the facility assess training needs of personnel on an ongoing basis?
- ★ Is there a training program for the IACUC members, especially the non-affiliated member?
- ★ Are there written guidelines and training for animal pain or distress assessment that is relevant to the research work at the facility?
- ★ Are investigators adequately training on how to conduct and document a search for alternatives to painful or distressful procedures?
- ★ Have protocols been developed for animals being used for procedure training for technicians or investigators?

A responsible training program should be in place at each research facility. Each training program may vary from one facility to another depending on the type of research being conducted and the needs of the facility. When a VMO reviews a training program, professional judgment is critical.

Documentation is important, but the "results" of a training program are the primary consideration.

# Training Bibliography

- Adsit, K.I., S.P. Tomasovic, A.J. Mastromarino, and K.N. Gray (1990). **Evaluation of the effectiveness of an animal care and use training program.** *Lab Animal* 19(4): 50, 52-54.  
NAL call number: QL55 A1L33  
Descriptors: University of Texas, training modules, training program assessment.
- American Association for Laboratory Animal Science (AALAS) (1991). **Training Manual Series , Volume III Laboratory Animal Technologist.** Cordova, Tennessee: AALAS.  
NAL call number: SF77 L26  
Descriptors: One of a series of manuals produced by AALAS to assist animal care personnel in obtaining certification at various levels of competence. Topics covered in this volume include" functions of management, identifying and controlling costs, regulations and security, scientific fundamentals in laboratory animal science, breeding and husbandry, laboratory animal environment, animal health, and research techniques, other manuals are available from AALAS through their website at [www.aalas.org](http://www.aalas.org)
- Anderson, L.C. and M.J. Brown (1990). **Training of animal care and use personnel: principles and program implementation.** In *Anesthesia and analgesia in laboratory animals proceedings -- 1990 Forum, American College of Laboratory Animal Medicine, Columbia Inn, Columbia, Maryland, May 3-6, 1990.* [Columbia, Md. : American College of Laboratory Animal Medicine, pp. 113-115.  
NAL call number: SF914 A53 1990  
Descriptors: training, technicians, animal husbandry.
- Bennett, B.T., M.J. Brown, and J.C. Schofield (1990). **Essentials for animal research. A primer for research personnel.** Beltsville, Maryland: Animal Welfare Information Center, 126 p.  
The full text document is available at  
<http://www.nal.usda.gov/awic/pubs/noawicpubs/essentia.htm>  
NAL call number: aQL55 B36 1994  
Descriptors: regulations, animal welfare, aseptic surgery, anesthesia, alternatives, animal care as an experimental variable, euthanasia, laboratory animals, techniques.
- bin Zakaria, M., N.W. Lerche, B.B. Chomel, and P.H. Kass (1996). **Accidental injuries associated with nonhuman primate exposure at two regional primate research centers (USA): 1988-1993.** *Laboratory Animal Science* 46(3): 298-304.  
NAL call number: 410.9 P94  
AB- Although occupationally acquired zoonoses of nonhuman primates have been well documented, the epidemiology of work-related injuries associated with occupational exposure to nonhuman primates has not been studied. To investigate such injuries, we retrospectively reviewed injury records at one regional primate research center and distributed a self-administered, anonymous questionnaire to at-risk personnel at two centers. Records of bite, animal-inflicted scratch, needle stick, cut, and mucous membrane exposure injuries were reviewed at one center for the 5-year period 1988 to 1993 to determine incidence and frequency of injuries and to identify possible risk factors. A total of 261 injuries were reported during this period, with an annual incidence for all injuries combined ranging from 43.5 to 65.5 injuries per 100,000 person workdays (pwd) at risk. For specific injuries the highest incidence was observed for animal-inflicted scratches and bites, with a rate of 82 and 81 per 100,000 pwd respectively. The job category Veterinary Resident was found to have the highest incidence for needle stick injuries (547 per 100,000 pwd), scratches (239 per 100,000 pwd), and cuts (171 per 100,000 pwd). The highest rates for bites were observed in the job categories Animal Health Technician and Animal Technician, with 171 and 150 per 100,000 pwd respectively; the category Staff Veterinarian had the highest rate of mucous membrane exposures (71 per 100,000 pwd). The frequency of all injuries was

greatest in personnel employed  $\leq 2$  years. Questionnaire responses indicated that having  $> 20$  h per week of contact with nonhuman primates or contact with more than 50 nonhuman primates per week was associated with a significantly increased risk of bites, animal-inflicted scratches, needle sticks, and mucous membrane exposures. In addition, data analysis indicated that under-reporting of work-related injuries was high; 59% of scratches, 50% of mucous membrane exposures, 45% of cuts, 37% of bites, and 20% of needle stick injuries went unreported. Results of this study identify job categories with a high incidence of specific injuries, for which additional targeted training and prevention programs may be beneficial, as well as providing quantitative baseline data for evaluating the effectiveness of any new safety programs or practices.

Descriptors: accidents, occupational statistics and numerical data, housing, animal statistics and numerical data, occupational diseases, epidemiology, primates wounds, bites, animal technicians, laboratory personnel, needle stick injuries epidemiology, primate diseases transmission, primates microbiology, retrospective-studies, risk-factors, zoonoses.

Bowd, A.D. (1998). **Animal care courses: Helping fulfill the mandate of animal care committees in Canada.** *Journal of Applied Animal Welfare Science* 1(4): 353-360.

NAL call number: HV4701 J68

Descriptors: ethics, alternatives, humane animal use, organization of animal care courses, training investigators, students, and IACUC members, topics covered include: regulations and legislation, ethical issues, alternatives, animal welfare, animal care, zoonoses and biohazards, animal surgery and euthanasia, practical handling of animals, improving statistical power, wildlife issues, case studies, teaching methods.

Duffee, N. (1999). **Alternative Training Methods I: Proceedings of the 1998 LAWTE Meeting.** *Lab Animal* 28(5): 24. Full-text article available at

<http://www.labanimal.com/iacuc/duffee0599.htm>

NAL call number: QL55 A1L33

AB- The author discusses alternative training methods presented at the 1998 meeting of the Laboratory Animal Welfare Training Exchange.

Descriptors: USDA training requirements, finding alternative training methods, simulation models, venipuncture, endotracheal intubation, surgical techniques, computer media, virtual reality, developing training programs.

Duffee, N. And M.T. Fallon (1998). **Researcher training: a new frontier.** *Lab Animal* 27(8):32-36.

NAL call number: QL55 A1L33

Descriptors: computer-based training materials, videotape, self-assessment web server, training researchers in animal care and use techniques, endotracheal intubation, project status.

Federation of European Laboratory Animal Science Associations (FELASA) (1999). **FELASA guidelines for education of specialists in laboratory animal science (Category D).**

*Laboratory Animals* 33(1): 1-15.

NAL call number: QL55 A1L3

Descriptors: category D corresponds to laboratory higher management, veterinarians, facility managers, etc., level of studies, specific requirements necessary for category D, detailed description of curriculum.

Federation of European Laboratory Animal Science Associations (FELASA) (1995). **FELASA recommendations on the education and training of persons working with laboratory animals: Categories A and C.** *Laboratory Animals* 29(2): 121-131.

NAL call number: QL55 A1L3

Descriptors: category A corresponds to laboratory animal technicians/technologists, category C corresponds to study directors, levels of certification, overview of duties and



responsibilities at different levels, animal care, animal husbandry, safety, legislation, responsibility for defined tasks and procedures, teaching syllabus and objectives.

Green, R.J. (1997). **Developing and implementing personnel safety programs. II. Safety training and education in animal research.** *Lab Animal* 26(6): 27 -30.

NAL call number: QL55 A1L33

Descriptors: laboratory hazards, animal experiments, biosafety, training, educational programs, laboratory workers.

Hutchison, J. (1989). **Thoughts on educating community members of animal care and use committees.** In *Science and Animals: Addressing Contemporary Issues* H.N. Guttman, J.A. Mench, and R.C. Simmonds (eds.), Bethesda, Maryland: Scientists Center for Animal Welfare, pp. 129-132.

NAL call number: HV4704 S33 1988

Descriptors: guidelines, public representation, educational programs.

Jennings, M. and P. Hawkins (1998). **Developing the ethics component of the U.K. modular training system for laboratory animal scientists: A LASA workshop report.** *Animal Welfare* 7(4): 445-458.

NAL call number:

AB-This paper presents the report of a LASA workshop on developing the ethics component of the UK modular training system for laboratory animal scientists. The objectives were: (i) to define and agree on the goals of ethics training; (ii) to set out means of achieving these goals in terms of an appropriate syllabus, effective approaches to training, and the resources necessary; (iii) to define the audience-who should be trained and to what level; and (iv) to consider the practicalities and means of assessment of prospective licensees. Although the focus was on the UK system, the issues are similar wherever ethics is taught in the laboratory animal context.

Jones, S.A. and T.J. Sharpe (1994). **An integrated training programme to meet UK guidelines for staff at all levels working with animals.** In *Welfare and science proceedings of the Fifth Symposium of the Federation of European Laboratory Animal Science Associations, 8-11 June 1993, Brighton, UK / Federation of European Laboratory Animal Science Associations Symposium* London: Royal Society of Medicine Press, pp. 363-364.

NAL call number: QL55 F43 1993

Descriptors: laboratory workers, training, laboratory animals, animal welfare, United Kingdom.

Maltby, C.J. (1989). **Partnership in training--a winning combination.** *Lab Animal* 18(5): 38-39.

NAL call number: L55 A1L33

Descriptors: laboratory animals, research institutes, educational programs.

National Academy of Sciences (1991). **Education and Training in the Care and Use of Laboratory Animals: A Guide for Developing Institutional Programs.** Washington, D.C.: Institute of Laboratory Animal Resources, 144 p.

NAL call number: SF604 E3

AB- The Committee on Education Programs in Laboratory Animal Science (EPLAS) has prepared this guide to aid institutions in implementing an education and training program that will meet the expectations of the Public Health Service (PHS). This guide was designed to fulfill several purposes. First, it is intended to assist institutional officials and institutional animal care and use committees (IACUCs) in determining the scope and depth of education training programs that will meet both institutional needs and the requirements of the PHS. Second, it is offered as a reference for the person or committee assigned the responsibility for coordinating these programs. Finally, portions of the guide will be useful to those people (content experts) who develop the material to be presented. To accommodate the diverse



backgrounds and needs of personnel, the committee has developed a multiphase program. Those topics considered essential elements for all personnel have been arranged into a single introductory module. The next three modules cover specific species, pain-management, and surgery. The next section of the guide contains detailed content outlines of the subjects covered in the four modules. The material in the modules is cross-referenced to appropriate subtopics in this section. Information on the following topics is provided: (1) laws, regulations, and policies that impact on the care and use of animals; (2) ethical and scientific issues; (3) alternatives to dissection; (4) responsibilities of the institution, the animal care and use committee, and the research and veterinary staffs; (5) pain and distress; (6) anesthetics, tranquilizers, analgesics, and neuromuscular blocking agents; (7) survival surgery and postsurgical care; (8) euthanasia; (9) husbandry, care, and the importance of the environment; and (10) a species-specific overview. The next section contains sources of information, selected bibliography, and audiovisual materials. The last section provides information on how to develop, deliver, and evaluate an educational program. Principles for the utilization and care of vertebrate animals used in testing, research, and training; a description of the Animal Welfare Information Center; and samples of learning objectives or self-assessment statements that coordinators may want to use or adapt for use at their institutions are appended.

Descriptors: anesthesiology, animal caretakers, animal husbandry, higher education, high schools, laboratory equipment, resource materials, science education, surgery, animal facilities, laboratory animals, research.

Scher, S. (1987). **Technician training: Animal care and use committees.** *Laboratory Animal Science* 37(special issue): 150-151.

NAL call number: 410.9 P94

Descriptors: laboratory animal science, animal welfare, education.

Simmonds, R.C. (1987). **Role of animal care and use committees in investigator training.** *Laboratory Animal Science* 37(special issue): 152-154.

NAL call number: 410.9 P94.

Descriptors: laboratory animals, animal welfare, educational programs.

Slack, G.N. (1996). **A summary of industry developed educational resources on food animal care and welfare.** In *Proceedings One-Hundredth Annual Meeting of the United States Animal Health Association, Excelsior Hotel, Little Rock, Arkansas, USA, 12-18 October 1996*, pp. 23-30.

Descriptors: livestock, education, resources, animal welfare, animal husbandry.

Smith, J.A. and M. Jennings (1998). **Ethics training for laboratory animal users.** *Laboratory Animals* 32(2): 128-136.

NAL call number: QL55 A1L3

AB- In the UK, all applicants for licences under the Animals (Scientific Procedures) Act 1986 must receive training in ethical aspects of laboratory animal use. There is, however, considerable uncertainty about the aims, suitable content and most appropriate means of delivery of such training. In this review a series of aims for licensee training in ethics are proposed, the key content is described and possible approaches to delivering such training are critically evaluated. Ethics training, it is argued, should: (i) be rooted in practice, focusing on the practical application of the Act to licensees' own work and encouraging them to take all possible steps to reduce or resolve any moral conflicts which the work entails; (ii) promote discussion, encouraging licensees to challenge their own views and critically appraise their work; and (iii) provide the necessary theoretical background to inform and stimulate such discussion. A variety of means of generating discussion and a range of practical considerations are explored.

Descriptors: ethics, animal welfare, training, laboratory animals, legislation, education, animal experiments.

- Stark, D.M. (1989). **The American veterinarians' role and education in laboratory animal science.** *Animal Technology: Journal of the Institute of Animal Technicians* 40(3): 199-201.  
NAL call number: QL55 I5  
Descriptors: laboratory animals, training, animal husbandry, ACUC.
- Sutherland, D.L. and D.R. Russell (1996). **Evolution of a training program built on employee involvement.** *Lab Animal* 25(9): 41-43.  
NAL call number: QL55 A1L33  
Descriptors: developing a training program at a large pharmaceutical facility, inclusion of veterinary care staff and training administrator in development process, subject matter experts, development of core modules—e.g., husbandry and care, development of species specific modules—e.g., rat, mouse, rabbits, development of task specific modules—e.g., handling and restraint, development of reference materials, teaching aids, curriculum, administration support, communication techniques within house to advertise the program, participant recognition program.
- Thomas, W.E., P.W. Lee, G.T. Sunderland, and R.P. Day (1996). **A preliminary evaluation of an innovative synthetic soft tissue simulation module ('Skilltray') for use in basic surgical skills workshops.** *Annals of the Royal College of Surgeons of England* 78(6 Suppl): 268-71.  
AB-The results of a preliminary evaluation comparing the relative merits of biological (freshly-prepared animal offal tissue) and synthetic (Skilltray) simulation modalities are presented, subsequent to their use during two basic surgical skills courses organised by The Royal College of Surgeons of England and The Royal College of Physicians and Surgeons of Glasgow in September 1995, and at which 18 SHO grade surgical trainees attended. Each trainee completed a questionnaire at the end of the first session on the second day of the course to assist the evaluation. Our conclusions were as follows: 1. The synthetic tissues evaluated provided a useful and functionally reproducible means for learning the basic exercises included in the mandatory skills course. 2. Freshly-prepared animal tissues undoubtedly provided a more "realistic" medium for rehearsing the basic surgical techniques taught. Trainees preferred to use the synthetic tissues initially and then to progress to the fresh equivalents subsequently. 3. The Skilltray provided all the requisite elements for rehearsing basic tissue handling, suturing, and anastomotic techniques in a self-contained, easily transportable module. We would suggest that such a unit be given to each participant to take away at the end of the basic skills course, to enable consolidation of the skills learned. 4. Where the use of fresh tissues is not possible the highly functional nature of the synthetic simulators evaluated make it acceptable then to use them as the only training modality.  
Descriptors: artificial organs, education, graduate methods, surgery education, teaching materials, attitude of personnel, evaluation studies, artificial skin, alternatives.
- Tomasovic, S.P., K.N. Gray, A.J. Mastromarino, and K.I. Adsit (1989). **Animal care and training for temporary research employees.** *Lab Animal* 18(4): 27-28,30,32.  
NAL call number: QL55 A1L33  
Descriptors: training programs, training, animal care and use, protocol, ACUC.
- University of Texas Health Science Center at San Antonio (1990). **Responsible care and use of animals in research and training : institutional animal care training program.** San Antonio, Texas: University of Texas Health Science Center, 36 p.  
NAL call number: HV4933 T4U5  
Descriptors: laboratory animals, animal welfare, animal models, bioethics.
- Van Hoosier, G.L. Jr., M.B. Dennis, Jr, C. Pekow, and C.S.Scott (1994). **Research animal management problems as a strategy for education and training.** *Contemporary Topics in Laboratory Animal Science* 33(5): 72-74.  
NAL call number: SF405.5 A23  
Descriptors: veterinary education, animal husbandry, training, educational methods.



- Van Hoosier, G.L. Jr., M.B. Dennis, Jr, C. Pekow, and C.S. Scott (1994). **Education and training through the use of problem-based learning exercises.** In *Welfare and science proceedings of the Fifth Symposium of the Federation of European Laboratory Animal Science Associations, 8-11 June 1993, Brighton, UK / Federation of European Laboratory Animal Science Associations Symposium*, London: Royal Society of Medicine Press, pp. 89-93.  
NAL call number: QL55 F43 1993  
Descriptors: veterinary education, teaching methods, research workers, discussion groups, animal welfare, class activities.
- White, G.L., M.A. Perry, and S.D. Kosanke (1991). **A comprehensive health science center educational program for animal care and use.** *Lab Animal* 20(7): 47-49.  
NAL call number: QL55 A1L33  
Descriptors: University of Oklahoma, course focus, workshops, laboratories.
- Will, J.A. and A. Gendron-Fitzpatrick (1987). **Investigator training: Animal care and use committees.** *Laboratory Animal Science* 37(special issue): 159-160.  
NAL call number: 410.9 P94  
Descriptors: animal welfare, continuing education, laboratory animals, research, universities, ACUC.
- Zutphen, B.F.M. van and J.B.F. van der Valk (1995). **Education and training: a basis for the introduction of the three Rs alternatives into animal research.** *Alternatives to Laboratory Animals: ATLA* 23(1): 123-127.  
NAL call number: Z7994.L3A5.  
AB- Education is a highly effective way of promoting the introduction of alternatives into the everyday practice of biomedical research and testing. In some countries, specific requirement for the education of persons involved in animal experimentation have been made compulsory by law. In The Netherlands, young scientists must take a course on laboratory animal science as part of, or in addition to, their biomedical graduate programme. This course provides information on the proper design of animal experiments, but also covers alternatives animal welfare issues and ethical aspects of animal experimentation. The Three RB of Russell & Burch are the guiding principles of the course, during which participants are challenged to seek methods or techniques that can replace, reduce or refine the use of animals. Since 1985 more than 2500 people in The Netherlands have taken the course, and evaluations have indicated that a large majority of the participants appreciated this education as a contribution to both the quality of experiments and the welfare of the animals, and considered the course to be indispensable for those who are responsible for the design and performance of animal experiments.  
Descriptors: animal testing alternatives, animal experiments, educational courses, training, laboratory animals, animal husbandry.

## Useful World Wide Web Sites

### American College of Laboratory Animal Medicine Autotutorials

<http://www.aclam.org/aclam/tutorial.htm#tutorial>

These completely new programs are a valuable source of teaching and visual material. Each program stands alone or may be used in conjunction with others in the series. Titles include: Dogs and Cats: Use in Research; Guinea Pig Series (4 programs); Laboratory Animals: Alternatives to Traditional Use; Laboratory Animals: Laws, Regulations and Guidelines; Mongolian Gerbils: Care, Diseases, and Use in Research; Nonhuman Primate Series (4 programs); Rabbit Series (6 programs); Rats and Mice Series (6 programs); Hamster Series (5 programs). Provides overview and ordering information.

**Arizona State University, User Training and Certification**  
[http://researchnet.vprc.asu.edu/animal\\_care/user\\_certification/](http://researchnet.vprc.asu.edu/animal_care/user_certification/)  
Nice example of on-line training at a university.

**IACUC Training and Learning Consortium**

[http://www.iacuc.org/training\\_general.html](http://www.iacuc.org/training_general.html)

Links to laboratory animal training sites at U.S. universities and to training media produced by various professional organizations and Federal agencies.

**Laboratory Animal Training Association**

<http://www.latanet.com>

Provides members with access to on-line training modules, a list of training videos available for purchase, an a buyers guide.

**Laboratory Animal Welfare Training Exchange (LAWTE)**

<http://www.lawte.org>

The Laboratory Animal Welfare Training Exchange is an organization of trainers, training coordinators and IACUC administrators. By sharing ideas on methods and materials for training, our members can learn together how best to meet the training and qualification requirements of national regulations and guidelines. For more detail look in the section on Organizations.

**The University of California, Davis, Autotutorials on the Web**

<http://clueless.ucdavis.edu/autotoot.html>

Tutorials on a variety of topics from the Animal Welfare Act to X-ray safety.

**University of Florida On-Line Training & Materials**

<http://nersp.nerdc.ufl.edu/~iacuc/Training.htm>

This is a collection of exams, slide shows, tutorials, texts, class notes, etc. that have been put on the web.

**University of Iowa, Animal Care Unit, Educational Resources**

<http://courses.uiowa.edu:8900/public/s0012/index.html>

An online investigator training program containing a course, quiz, glossary, bulletin board, and fact sheets on subjects ranging from blood sampling in rodents to euthanasia.

**University of Texas Health Science Center at San Antonio - Laboratory Animal Programs, Institutional Animal Care Training Program**

<http://oerweb.uthscsa.edu/iphccla/requirem.htm>

This site provides a training program overview.





# Whistleblowing





# Department of Health and Human Services, Office of Research Integrity Guidelines for Institutions and Whistleblowers: Responding to Possible Retaliation Against Whistleblowers in Extramural Research (November 20, 1995)

This document can be found at <http://ori.dhhs.gov/guidelin.htm>

*Editor's Note: These guidelines were developed to provide guidance to research institutions in handling allegations of scientific misconduct. "Scientific misconduct" means fabrication, falsification, plagiarism, or other practices that seriously deviate from those that are commonly accepted within the scientific community for proposing, conducting, or reporting research. It does not include honest error or honest differences in interpretations or judgments of data. It does not include violations of USDA's animal welfare regulations or the PHS policy on the care and use of laboratory animals. However, they may provide guidance to animal care programs in the establishment of whistleblower guidelines.*

## I. INTRODUCTION

The Office of Research Integrity (ORI), Department of Health and Human Services (DHHS), strongly believes in the importance of protecting whistleblowers who make good faith allegations of scientific misconduct to ORI or appropriate institutional authorities. In particular, ORI is committed to protecting good faith whistleblowers from retaliation by covered institutions and their members.

By regulation, each extramural entity that applies for a biomedical or behavioral research, research-training, or research-related grant or cooperative agreement under the Public Health Service (PHS) Act must establish policies and procedures that provide for "undertaking diligent efforts to protect the positions and reputations of those persons who, in good faith, make allegations." 42 C.F.R. Part 50.103(d)(13).

Although the regulation does not provide specific direction on how to protect whistleblowers, ORI has determined that adherence to the policies and procedures set forth in these Guidelines is one method of satisfying the requirements of the regulation. ORI will recognize an institution's substantial conformity with these Guidelines as meeting the whistleblower protection requirement of 42 C.F.R. Part 50.103(d)(13). Specifically, each institution which substantially adheres to Sections IV and V of these Guidelines in responding to whistleblower retaliation complaints will be considered in compliance with the regulatory whistleblower protection requirement for resolution of retaliation complaints. However, institutions are free to disregard these Guidelines and adopt other procedures that conform to the regulatory requirement.

If an institution elects to adopt these Guidelines, it must abide by each provision that uses the operative word "shall." On the other hand, provisions which employ the words "should" or "may" are merely practical suggestions. An institution will not be out of conformity with the Guidelines if it fails to carry out these recommendations. Rather, an institution may substitute for these suggested provisions alternative procedures that are consistent with the mandatory provisions of these Guidelines and the regulatory whistleblower protection provisions.

In addition to the requirements of 42 C.F.R. Part 50.103(d)(13), ORI encourages covered institutions to adopt policies and procedures that conform to PHS Act Part 493(e), a whistleblower protection



statute enacted by Part 163 of the National Institutes of Health Revitalization Act of 1993, although Part 493 has not been implemented by regulation at the time of issuance of these Guidelines. Besides protecting good faith allegations of scientific misconduct, PHS Act Part 493(e) mandates the protection of whistleblowers for (1) good faith allegations of an inadequate institutional response to scientific misconduct allegations and (2) good faith cooperation with investigations of such allegations. The statute covers allegations of misconduct which involve research or research related grants, contracts or cooperative agreements under the PHS Act. ORI also encourages institutions to adopt principles consistent with the Whistleblower Bill of Rights (Appendix A) recommended by the Commission on Research Integrity and to foster institutional commitment to those principles. The specific principles of the Whistleblower Bill of Rights are as follows:

- (1) whistleblowers are free to disclose lawfully whatever information supports a reasonable belief of research misconduct as it is defined by PHS policy,
- (2) institutions have a duty not to tolerate or engage in retaliation against good-faith whistleblowers,
- (3) institutions have a duty to provide fair and objective procedures for examining and resolving complaints, disputes and allegations of research misconduct,
- (4) institutions have a duty to follow procedures that are not tainted by partiality arising from personal or institutional conflict of interest or other sources of bias,
- (5) institutions have a duty to elicit and evaluate fully and objectively information about concerns raised by whistleblower,
- (6) institutions have a duty to handle cases involving alleged research misconduct as expeditiously as possible without compromising responsible resolutions, and
- (7) at the conclusion of proceedings, institutions have a responsibility to credit promptly, in public or private as appropriate, those whose allegations are substantiated.

These Guidelines are consistent with the rights and responsibilities enumerated in the Whistleblower Bill of Rights.

While compliance with these Guidelines will satisfy the existing regulatory requirements at 42 C.F.R. Part 50.103 (d)(13), this publication does not bind the Department in any way as to the substantive provisions of the forthcoming new regulation implementing the whistleblower protection statute, PHS Act Part 493(e).

## **II. PURPOSE**

The purpose of these Guidelines is to set forth ORI's suggested approach for handling whistleblower retaliation cases which arise at covered institutions. Substantial adherence to the Guidelines in each whistleblower case affords a "safe harbor" in which conforming institutions will be deemed in compliance with Part 50.103(d)(13) of the scientific misconduct regulation. For those institutions which adopt alternative procedures to comply with the regulation, ORI may review those cases which do not abide by these Guidelines to determine whether an institution has taken diligent efforts to protect the positions and reputations of good faith whistleblowers.

These Guidelines also provide information to whistleblowers on an appropriate method of submitting retaliation complaints and subsequent procedures for resolving the complaints. ORI encourages whistleblowers to refer institutions to these Guidelines when making specific complaints of retaliation.

These Guidelines apply to all instances of possible retaliation against whistleblowers whose allegation of scientific misconduct is covered by 42 C.F.R. Part 50, Subpart A.

### III. DEFINITIONS

"Adverse action" means any action taken by a covered institution or its members which negatively affects the terms or conditions of the whistleblower's status at the institution, including but not limited to his or her employment, academic matriculation, awarding of degree, or institutional relationship established by grant, contract or cooperative agreement.

"Allegation" means any disclosure, whether by written or oral statement, or any other communication, to an institutional, a Department of Justice (DOJ), or a DHHS official who receives the allegation while acting in their official capacity, that a covered institution or member thereof has engaged in scientific misconduct. Allegations made to any of the above officials may be in conjunction with communications to Congress (1).

"Arbitration" means the process described in this Part through which an unresolved dispute regarding whistleblower retaliation is submitted to an arbitrator for a final and binding decision.

"Arbitrator" means one or more impartial persons selected according to the rules of a designated arbitration association who shall hear and decide whistleblower retaliation complaints under this Part.

"Covered institution" means any entity, whether individual or corporate, which applies for or receives funds under a research, research-training, or research-related grant or cooperative agreement under the PHS Act.

"Deciding official" means the official designated by the administrative head of a covered institution to make a final institutional determination as to whether retaliation occurred.

"Good faith allegation" means an allegation of scientific misconduct made with a belief in the truth of the allegation which a reasonable person in the whistleblower's position could hold based upon the facts. An allegation is not in good faith if made with reckless disregard for or willful ignorance of facts that would disprove the allegation

"Institutional member, or member" means a person who is employed by, affiliated with under a contract or agreement, or under the control of a covered institution. Institutional members include but are not limited to administrative, teaching and support staff, researchers, clinicians, technicians, fellows, students, and contractors and their employees.

"Office of Research Integrity (ORI)" means the office to which the Secretary has delegated responsibility for addressing scientific misconduct issues related to PHS activities, including the protection of good faith whistleblowers.

"Responsible official" means the official designated by and reporting to the administrative head of a covered institution to establish and implement the institution's whistleblower policies.

"Retaliation" means any adverse action or credible threat of an adverse action taken by a covered institution, or member thereof, in response to a whistleblower's good faith allegation of scientific misconduct. It does not include an institution's decision to investigate a good faith allegation of scientific misconduct.

"Scientific misconduct" means fabrication, falsification, plagiarism, or other practices that seriously deviate from those that are commonly accepted within the scientific community for proposing,

conducting, or reporting research. It does not include honest error or honest differences in interpretations or judgments of data.

"Whistleblower" means an individual who makes an allegation or demonstrates an intent to make an allegation (or what is perceived to be an allegation) while a member of the institution at which the alleged scientific misconduct occurred.

## **IV. PROCESSING WHISTLEBLOWER RETALIATION COMPLAINTS**

### **A. Responsible Official**

1. Covered institutions shall designate a "responsible official" to establish and implement the institution's whistleblower policies according to 42 C.F.R. Part 50.103(d)(13) and these Guidelines. The responsible official also serves as a liaison between the institution and ORI for transmitting such information as ORI may require.

2. The responsible official shall be free of any real or apparent conflicts of interest in any particular case.

3. If involvement of the responsible official in a particular case creates a real or apparent conflict of interest with the institution's obligation to protect good faith whistleblowers, and the conflict cannot be satisfactorily resolved for that case, the administrative head of the institution shall appoint a substitute responsible official who has no conflict of interest.

### **B. Notice of Institutional Policy**

The institution shall provide to all its members notice of its whistleblower policies and these Guidelines with Appendices. The notice shall include the requirement set forth below regarding a whistleblower's deadline for filing a retaliation complaint. The institution's policies and these Guidelines shall be either disseminated or be publicized and made readily available to all institutional members.

### **C. Filing Complaints**

1. A whistleblower who wishes to receive the procedural protections described by these Guidelines shall file his or her retaliation complaint with the responsible official at the appropriate institution within 180 days (2) from the date the whistleblower became aware or should have become aware of the alleged adverse action. Covered institutions shall review and resolve all whistleblower retaliation complaints and should do so within 180 days after receipt of the complaint. If the whistleblower fails to receive an institutional response to the complaint in accordance with these Guidelines within ten (10) working days (3), the whistleblower may file the retaliation complaint directly with ORI at the following address:

Office of Research Integrity  
Division of Policy and Education  
5515 Security Lane, Suite 700  
Rockville, MD 20852  
Telephone: (301) 443-5300  
Fax: (301) 594-0042

ORI will forward such complaints to the institution's responsible official for appropriate action.

2. In addition to prospective complaints, institutions may apply these Guidelines to complaints of retaliation made prior to the effective date of the institution's adoption of these Guidelines.



3. The retaliation complaint must include a description of the whistleblower's scientific misconduct allegation and the asserted adverse action, or threat thereof, against the whistleblower, by the institution or its members in response to the allegation. If the retaliation complaint is incomplete, the responsible official shall describe to the whistleblower what additional information is needed in order to meet the minimum requirements of a complaint under this Part.

#### **D. Responding to Complaints**

1. Upon receipt of a whistleblower retaliation complaint, the responsible official shall notify the whistleblower of receipt within ten (10) working days (4) after receipt. The notice shall also inform the whistleblower of which process under Section V of the Guidelines the institution proposes to follow in resolving the retaliation complaint and the necessary actions by the whistleblower required under that process. The notice shall also notify the whistleblower of his or her choice of responses listed below.

2. The whistleblower may raise any concerns about the proposed process with the responsible official and the institution may modify the process in response to the whistleblower's concerns.

3. The whistleblower has five working days from the date of receipt of the initial notification in Part 1 above to:

a. accept the proposed process, although the whistleblower may also submit documentation for the official record about any concerns he or she may have about the proposed process; or

b. not accept the proposed process. If the whistleblower rejects the proposed process, he or she may pursue other remedies as provided by law.

4. If the whistleblower does not accept the proposed process, the institution may, but is not required to, propose the alternative option under Section V of the Guidelines.

5. The institution shall notify ORI of any whistleblower retaliation complaint it receives within ten (10) working days (5) after receipt of the complaint.

#### **E. Interim Protections**

1. At any time before the merits of a whistleblower retaliation complaint have been fully resolved, the whistleblower may submit a written request to the responsible official to take interim actions to protect the whistleblower against an existing adverse action or credible threat of an adverse action by the institution or member.

2. Based on the available evidence, the responsible official shall make a determination of whether to provide interim protections and shall advise the whistleblower of his or her decision in writing. Documentation underlying the decision whether to provide interim protections shall become part of the record of the complaint. When the whistleblower retaliation complaint is fully resolved, any temporary measure taken to protect the whistleblower shall be discontinued or replaced with permanent remedies.

#### **V. RESOLUTION OF COMPLAINTS**

1. For each whistleblower retaliation complaint received, a covered institution shall adhere to one of the two alternative processes for resolving the whistleblower retaliation complaint, or settle the complaint, as described below.

2. Whichever process is elected shall be implemented in a timely fashion. The process should be completed within 180 days of the date the complaint is filed, unless the whistleblower agrees to an



extension of time. The institution shall promptly report the final outcome of either process or any settlement to ORI.

3. If the whistleblower declines the institution's proposed process according to these Guidelines, he or she may pursue any other legal rights available to the whistleblower for resolution of the retaliation complaint. However, ORI will deem the institution to have met its obligation under 42 C.F.R. Part 50.103(d)(13) and will not pursue the whistleblower complaint further.

### **Option A: Institutional Investigation**

1. If the institution elects Option A, the institution shall conduct an investigation of the whistleblower retaliation complaint according to these Guidelines and implement appropriate administrative remedies consistent with the investigation's finding and institutional decision thereon.

2. An investigation of whistleblower retaliation shall be timely, objective, thorough, and competent. The investigation should be conducted by a panel of at least three (3) individuals appointed by the responsible official. The members of the investigation panel, who may be from outside the institution, shall have no personal or professional relationship or other conflict of interest with the whistleblower or the alleged individual retaliator(s), and shall be qualified to conduct a thorough and competent investigation.

3. The investigation shall include the collection and examination of all relevant evidence, including interviews with the whistleblower, the alleged retaliator(s), and any other individual who can provide relevant and material information regarding the claimed retaliation.

4. The institution shall fully cooperate with the investigation and use all available administrative means to secure testimony, documents, and other materials relevant to the investigation.

5. The confidentiality of all participants in the investigation shall be maintained to the maximum extent possible throughout the investigation.

6. The Panel members shall evaluate and respond objectively to any concerns raised by the whistleblower about the process, including concerns regarding the selection of the deciding official, responsible official and specific panel members, which are raised prior to resolution of the complaint.

7. The conclusions of the investigation shall be documented in a written report and made available to the whistleblower. The report shall include findings of fact, a list of witnesses interviewed, an analysis of the evidence, and a detailed description of the investigative process.

8. The deciding official shall make a final institutional determination as to whether retaliation occurred. This decision shall be based on the report, the record of the investigation, and a preponderance of evidence standard.

9. If there is a determination that retaliation has occurred, the deciding official shall determine what remedies are appropriate to satisfy the institution's regulatory obligation to protect whistleblowers. The deciding official shall, in consultation with the whistleblower, take measures to protect or restore the whistleblower's position and reputation, including making any public or private statements, as appropriate. In addition, the deciding official may provide protection against further retaliation by monitoring or disciplining the retaliator.

10. The institution shall promptly notify ORI of its conclusions and remedies, if any, and forward the underlying investigation report to ORI.

11. The ORI will review the institutional report to determine whether the institution has substantially followed the process described herein. If the institution has substantially conformed to the process, ORI will not review the merits of the institutional determination under Paragraphs 8 and 9.

12. Institutional compliance with Option A does not bar the whistleblower from seeking redress against the institution's decision under Paragraph 8 and 9, under State law, institutional procedure, policy or agreement, or as otherwise provided by law.

### **Option B: Arbitration**

1. If the institution elects Option B, the institution shall offer the whistleblower the opportunity to submit the retaliation dispute to binding arbitration. The parties shall sign a written agreement that the retaliation dispute will be decided by final and binding arbitration, identifying the person who shall conduct the arbitration.

2. The arbitration agreement shall specify that the institution and the whistleblower abrogate all other rights under Federal, State and local law, and other institutional policies or employment agreements pertinent to the resolution of the whistleblower retaliation complaint, other than enforcement of the arbitration award. However, the parties may enter into any legally enforceable settlement agreement before a final arbitration award is made. A sample arbitration agreement is attached at Appendix B.

3. Any retaliation complaint submitted to arbitration shall be arbitrated according to the rules and procedures of the presiding arbitrator and designated arbitration association.

4. An arbitration under these Guidelines shall be conducted by an arbitrator who has no personal or professional relationship or conflict of interest with the whistleblower, the institution, the alleged retaliator(s), or any person who is the subject of the underlying scientific misconduct allegation. The institution and the whistleblower shall agree on the choice of arbitrator. The arbitration should be facilitated by the American Arbitration Association or any other recognized non-profit arbitration association.

5. The institution and the whistleblower shall share equally the administrative costs of the arbitration. Each party is responsible for the cost of presenting its own case.

6. The arbitration agreement shall specify that the arbitrator shall require the institution to compensate the whistleblower for part or all of his or her arbitration costs, including attorney fees, if the arbitrator finds that the institution, or its members, retaliated against the whistleblower.

7. The arbitration agreement shall also specify that the arbitrator shall require the whistleblower to compensate the institution for part or all of any filing fees and arbitrator's costs if the arbitrator finds that the whistleblower's allegation of scientific misconduct was not made in good faith. If an institution seeks compensation on this basis, it shall make a preliminary motion to dismiss the retaliation complaint prior to commencement of a hearing. The arbitrator shall, if possible, make a threshold decision on the question of good faith based on written submissions prior to commencement of a hearing on the merits of the retaliation dispute. The institution has the burden of proving by a preponderance of the evidence that the allegation of scientific misconduct was not made in good faith.

8. The arbitration agreement shall specify a preponderance of the evidence standard in determining whether retaliation occurred or any other standard mutually agreed to by the parties.

9. The arbitration agreement shall state that the arbitrator's award is final and binding on all parties, and enforceable as provided by law.

10. If the arbitrator finds that the institution, or its members, retaliated against the whistleblower, the arbitrator may order any relief necessary to make the whistleblower whole for the direct or indirect consequences of retaliation, including protection against further retaliation through imposing a system to monitor or discipline the retaliator. The institution shall abide by the arbitrator's final award and shall implement any additional administrative actions it determines is necessary to correct the retaliation.

11. The institution shall promptly forward a copy of the final arbitration award to ORI.

### **C. Settlement**

In lieu of the two options described above, an institution and whistleblower may, at any time after the retaliation complaint is made, enter into any binding settlement agreement which finally resolves the retaliation complaint. If both parties agree, the responsible official shall facilitate negotiation of such settlements. If such an agreement is reached, the institution and the whistleblower shall sign a statement indicating that the retaliation complaint has been resolved. The institution shall within 30 days send a copy of the signed statement to ORI. ORI does not require a copy of the actual terms of the settlement. The settlement may not restrict the whistleblower from cooperating with any investigation of an allegation covered by 42 C.F.R. Part 50, Subpart A. ORI shall consider a settlement meeting these requirements as fulfilling the institution's regulatory obligation under 42 C.F.R. Part 50.103(d)(13).

## **VI. INSTITUTIONAL COMPLIANCE**

At any time ORI may review a covered institution's compliance with 42 C.F.R. Part 50.103(d)(13) and these Guidelines to the extent that the institution relies on these Guidelines for regulatory compliance. Covered institutions and their members shall cooperate with any such review and provide ORI access to all relevant records. If a covered institution's procedures and implementation thereof substantially conforms to Sections IV and V above, it shall be deemed to have met its whistleblower protection obligation under 42 C.F.R. Part 50.103(d)(13).

### **Footnotes:**

- (1) Communications to Congress must be made in a way that affords "affected individual(s) confidential treatment to the maximum extent possible" consistent with 42 C.F.R. 50.103 (d)(3).
- (2) The institution may establish a longer period of time.
- (3) The institution may establish a shorter period of time.
- (4) The institution may establish a shorter period of time consistent with footnote 2.
- (5) The institution may establish a shorter period of time.



## APPENDIX A

# Responsible Whistleblowing: A Whistleblower's Bill of Rights

a. **Communication:** Whistleblowers are free to disclose lawfully whatever information supports a reasonable belief of research misconduct as it is defined by PHS policy. An individual or institution that retaliates against any person making protected disclosures engages in prohibited obstruction of investigations of research misconduct as defined by the Commission on Research Integrity. Whistleblowers must respect the confidentiality of sensitive information and give legitimate institutional structures an opportunity to function. Should a whistleblower elect to make a lawful disclosure that violates institutional rules of confidentiality, the institution may thereafter legitimately limit the whistleblower's access to further information about the case.

b. **Protection from retaliation:** Institutions have a duty not to tolerate or engage in retaliation against good-faith whistleblowers. This duty includes providing appropriate and timely relief to ameliorate the consequences of actual or threatened reprisals, and holding accountable those who retaliate. Whistleblowers and other witnesses to possible research misconduct have a responsibility to raise their concerns honorably and with foundation.

c. **Fair procedures:** Institutions have a duty to provide fair and objective procedures for examining and resolving complaints, disputes, and allegations of research misconduct. In cases of alleged retaliation that are not resolved through institutional intervention, whistleblowers should have an opportunity to defend themselves in a proceeding where they can present witnesses and confront those the charge with retaliation against them, except when they violate rules of confidentiality.

Whistleblowers have a responsibility to participate honorably in such procedures by respecting the serious consequences for those they accuse of misconduct, and by using the same standards to correct their own errors that they apply to others.

d. **Procedures free from partiality:** Institutions have a duty to follow procedures that are not tainted by partiality arising from personal or institutional conflict of interest or other sources of bias. Whistleblowers have a responsibility to act within legitimate institutional channels when raising concerns about the integrity of research. They have the right to raise objections concerning the possible partiality of those selected to review their concerns without incurring retaliation.

e. **Information:** Institutions have a duty to elicit and evaluate fully and objectively information about concerns raised by whistleblowers. Whistleblowers may have unique knowledge needed to evaluate thoroughly responses from those whose actions are questioned. Consequently, a competent investigation may involved giving whistleblowers one of more opportunities to comment on the accuracy and completeness of information relevant to their concerns, except when they violate rules of confidentiality.

f. **Timely processes:** Institutions have a duty to handle cases involving alleged research misconduct as expeditiously as is possible without compromising responsible resolutions. When cases drag on for years, the issue becomes the dispute rather than its resolution. Whistleblowers have a responsibility to facilitate expeditious resolution of cases by good-faith participation in misconduct procedures.

g. **Vindication:** At the conclusion of proceedings, institutions have a responsibility to credit promptly--in public and/or in private as appropriate--those whose allegations are substantiated.

Every right carries with it a corresponding responsibility. In this context, the Whistleblower Bill of Rights carries the obligation to avoid false statements and unlawful behavior.





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AB: Uncovering misconduct in science, like misconduct in other areas of industry and government activities, often depends on the willingness of those aware or suspecting misconduct to report it. Uncovering such misconduct is generally recognized to be of significant value to society and to the integrity of scientific research. However, the willingness of individuals to allege misconduct is likely to depend on how the system deals with and protects them when they come forth with their allegations. Potential whistleblowers must consider whether the allegation will be taken seriously and the report treated confidentially and whether reporting will provoke retaliation not only from those accused but also from the larger academic and scientific community.
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 Descriptors: first nationwide study of whistleblowers (N = 300) in the US, data indicate that employees are often punished for bringing forth valid information about wrongdoing or illegal conduct, organizations that publicly say that they want employees to "participate" & that they hold high ethical standards generally move to discredit the whistleblower & to fire them as soon as they see that they have information about waste, fraud, or abuses of power in the organization. The causes, nature, & consequences of management retaliation against whistleblowers in all types of work settings are discussed, organizational crime, ethics, sanctions.
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## Useful World Wide Web sites

### Emory University School of Medicine- Institutional Animal Care and Use Committee

<http://www.emory.edu/WHSC/MED/IACUC/reporting.htm>

Standard Operating Procedure for reporting incidents of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals.

### Government Accountability Project

<http://www.whistleblower.org/>

Resources for whistleblowers, information on current Federal regulations protecting whistleblowers, general articles, etc.

### Municipal Research and Services Center-A resource for Washington local governments

<http://www.mrsc.org/library/compil/cpwhist.htm>

The ordinance and policy provisions contained in this compilation are offered as samples rather than models.

### National Whistleblower Center

<http://www.whistleblowers.org>

The National Whistleblower Center is an educational and advocacy organization committed to government accountability and protecting the rights of employee whistleblowers.

**U.S. Department of Health and Human Services, Office of Research Integrity**

<http://ori.dhhs.gov/whistle.htm>

Provides information on whistleblower issues.

**University of Arizona Institutional Animal Care and Use Committee**

<http://www.ahsc.arizona.edu/uac/iacuc/special.shtml#invest>

A special policy on the investigation of concerns involving the care and use of animals.

**University of California at Irvine**

<http://www.abs.uci.edu/depts/mailrec/uci-ppm/whisblow.html>

Example of policies and guidelines implemented by an academic research institution

**University of Tennessee, Office of Laboratory Animal Care**

<http://www.ra.utk.edu/ora/labaniml/noncompl.html>

Policy for reporting noncompliance with laboratory animal care and use guidelines.





# **Membership Issues and IACUC Communications**





# Appointing Animal Protectionists to Institutional Animal Care and Use Committees

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## INTRODUCTION

In 1985, the U.S. Congress passed two laws requiring facilities that conduct biomedical research on animals to establish what later came to be called "institutional animal care and use committees" (IACUCs). These laws were the Health Research Extension Act (HREA) (11) and the Improved Standards for Laboratory Animals Act (ISLA) (10). The ISLA, enacted as part of that year's farm bill, was actually a set of amendments to the Animal Welfare Act (AWA). Both the HREA and AWA amendments mandated that IACUCs review proposals for research and periodically inspect research facilities, among other activities.

In 1986, the Public Health Service (PHS) implemented the HREA by issuing a revised "Policy on Humane Care and Use of Laboratory Animals" (5). The U.S. Department of Agriculture (USDA) implemented the AWA amendments by issuing final regulations in 1989 (13). Thus, research facilities have been legally obligated to operate IACUCs for several years. A few institutions, anticipating the benefits of having an IACUC, voluntarily established IACUC-like committees long before Congress took action (7).

Both the HREA and AWA amendments stipulated that IACUCs include at least one member who is not otherwise affiliated with the facility. The AWA amendments went further by indicating that the non-affiliated members (NAMs) were to provide "representation for general community interests in the proper care and treatment of animals." Animal protectionists<sup>1</sup> hoped that this mandate would provide a public window into the workings of research laboratories, a step toward both more accountability from researchers and better treatment for animals. In their view, the best candidates for the NAM position are local individuals who already have a track record in animal protection and who could be regarded as representing the research animals, and the public's concern for those animals, rather than the institution itself.

Animal protectionists are not likely to regard NAMs who lack a track record in animal advocacy as credible watchdogs over the facility's treatment of animals.

On the other hand, many in the research community viewed the NAM mandate as inappropriate, if not punitive. In their view, selecting NAMs should be done with the utmost care, to screen out individuals hostile to animal research who would disrupt meetings, leak confidential information, and commit other transgressions (2, 9).

This clash of views has wound up being decided in favor of the research facilities themselves, which alone are vested with the authority to appoint NAMs and other IACUC members. Thus the community has no say in determining who their committee representative will be.

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<sup>1</sup>We use the phrase "animal protectionist" instead of the narrower "animal rightist" to refer to animal advocates who may or may not believe in the philosophy of animal rights and in the complete abolition of vivisection.



Very little is known, apart from anecdotes, about the types of individuals being selected to serve as NAMs. The main reason is that facilities usually have tried to keep the identity of their NAMs confidential, reflecting the charged political climate surrounding animal research issues.<sup>2</sup> From the information that is available, it seems clear that facilities typically have selected individuals not known within their community as advocates for animals (6). This is not to say that the typical NAM has no concern for animal welfare, only that such concern, if present, would not be apparent to outside observers. Thus, individuals in the community who care about the treatment of research animals typically have no reason to believe that the NAM is a strong advocate for animals. These individuals also have no straightforward way of knowing if their concerns are being raised by the NAM.

Of course, some facilities are either more conservative or progressive than the typical scenario described above. Some facilities not only avoid appointing community-based animal advocates to IACUCs and keep the identity of their NAMs confidential, they go so far as to strain the letter or spirit of the law. They appoint people who are either currently affiliated with the institution in question or formerly affiliated (e.g., alumnus, former employee). Some NAMs have been scientists from nearby research institutions or staff of pro-vivisection organizations.

On the other hand, some progressive institutions have appointed prominent animal welfarists to serve as NAMs. Two of our colleagues at The Humane Society of the United States (HSUS) served as NAMs on IACUCs at large state universities. F. Barbara Orlans identified two institutions that have published policies explicitly calling for community-recognized animal welfarists on their IACUCs, namely, the Wisconsin Regional Primate Research Center (whose policy refers to "advocates of animal rights") and the University of Southern California ("a public member representing the animal advocate community") (6).

It is not difficult to account for the prevailing tendency of research facilities to "play it safe" by appointing NAMs who have no track record in animal welfare advocacy, and to withhold the identities of these individuals from the very people whom they are supposed to represent. At least initially, many scientists resented the call for community representatives to serve on IACUCs (as well as IACUCs themselves). At issue was not only the wisdom of having someone on the committee who was not likely to be a fellow scientist, but also the implication of having an outsider sit on the committee (i.e., couldn't the researchers themselves and their institutional colleagues be trusted?). Moreover, NAMs were not just any outsiders; they were animal welfare watchdogs. Thus the NAM role has been caught up in the polarization between the animal research and animal protection communities. Some research facilities and individual scientists feel under siege from animal rights activists and the research community has devoted considerable resources and attention to keeping these activists at bay, such as by enhancing building security. The last thing these facilities and scientists want to do is bring into their IACUC deliberations someone who is considered the enemy, or at least a troublemaker.

## **A PROPOSAL**

It has been several years since most research facilities established IACUCs. Many researchers and their institutions have come to accept the value of IACUCs in not only helping to ensure the least harm to the least number of animals, but also in helping to improve the scientific quality of proposals, to assure compliance with existing regulations, and to keep the institution's animal care and use program above reproach on animal welfare issues.

Similarly, most researchers and facilities have come to accept the role of NAMs. They recognize that times have changed, the public is concerned about the care and treatment of animals in labs, and having NAMs on IACUCs is a small price to pay for continued public support for animal

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<sup>2</sup>It is a little known fact that the names of the NAMs and other ACUC members are available to the public under the Freedom of Information Act (FOIA). These names are listed on the Animal Welfare Assurances that facilities submit to the PHS. When responding to FOIA requests, the PHS prefers to delete these names, but when pressed, will release them.

research. Moreover, even though non-scientists may be ill-equipped to grapple with the technical details of research proposals, there is a growing

recognition that they can raise fundamental questions that might not otherwise be addressed (9).

At the same time as researchers have come to accept the importance of IACUCs, the hostility between the scientific and animal protection communities is beginning to subside, with some members of each community starting to focus on areas of common interests, rather than points of disagreement (16).

The time is ripe for research facilities to be less conservative in their appointments of NAMs. In light of the strides being made in bridging the gap between the scientific and animal protection communities, we propose that animal research facilities, as a show of good-will, voluntarily appoint individuals to their IACUC who are recognized within the local community as advocates for animals. We also propose that these individuals be encouraged to serve openly as a liaison between the research community and the concerned public, neither as mouthpieces for the facility nor as spies for local animal activists, but as credible advocates for animals seeking to function within an imperfect oversight mechanism that has built-in tensions and ambiguities.

We further recommend that facilities appoint at least two such animal protectionists to their IACUCs, so that when one cannot attend a particular meeting, at least the other can be present. In Orleans' recent survey of ten IACUC chairpersons, half of the respondents indicated that "non-attendance of their community member had been a real problem and most [chairpersons] expressed dismay at this" (6, p. 114). In light of this problem, which seems inevitable to a greater or lesser greater extent, complying with the spirit of the AWA for community representation all but necessitates having two or more NAMs.<sup>3</sup>

Some community-recognized animal advocates may be students or employees of their local research facility, and would thereby be affiliated with the institution. Such institutions are free to appoint these advocates to their IACUC (though not as NAMs); however, because of conflict of interest, this would not provide the kind of community representation that we are proposing.

Federal law does not require that IACUCs include individuals who have demonstrated their care and concern for animals in the local community.<sup>4</sup> However, Congress gave NAMs a unique role by stipulating that they represent general community interests in the proper treatment of animals. To be sure, all IACUC members can be considered as advocates for the institution's research animals by virtue of serving on the committee. However, only the NAM's role is linked to community representation and is free of the potential for conflict of interest due to affiliation with the institution.

Unfortunately, the legislative history of the 1985 amendments to the AWA does not shed much light on what motivated Congress to stipulate a role for community representatives in IACUC activities. Clearly, however, Congress believed it was important to open up IACUC deliberations to input and scrutiny from individuals who had no vested interest in the research facilities in question. Moreover, that input and scrutiny was intended to have a certain orientation, i.e., to help ensure the

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<sup>3</sup>The influence of even two NAMs would be diluted in large committees. In such cases, facilities should appoint NAMs in numbers sufficient to maintain the balance among IACUCs members implied in the congressional legislation.

<sup>4</sup>The AWA does require a minimum of one NAM and two affiliated members, one of whom must be a veterinarian. The PHS Policy calls for a minimum of one NAM and four affiliated members, including a veterinarian with training or experience in laboratory science and medicine, a practicing scientist experienced in animal research, and a member whose primary concerns are in a non-scientific area, for example an ethicist, lawyer, or member of the clergy.



proper treatment of animals. What better way to ensure this, and to embrace the spirit of the AWA amendments, than to fill this role with someone who not only has care and concern for animals, but who also has a track record of animal welfare activity in the community and is willing to serve openly as the community's representative on animal welfare concerns?

Skeptics may view our proposal as either hopelessly naive given the persistent controversy over animal research, or as a thinly-veiled attempt to subvert the IACUCs' workings. We argue below that appointing animal advocates to IACUCs and having them be a bridge between the research facility and concerned public, when carried out with common sense, engenders little risk but has significant benefit.

## **ADVANTAGES OF APPOINTING ANIMAL PROTECTIONISTS TO IACUCS**

All positions on IACUCs, including the NAM, should be filled only after careful deliberation. We recognize that facilities will want to be especially careful if they choose to appoint individuals who have a track record for animal advocacy within the local community. These facilities will no doubt seek to appoint pragmatists willing to work within the system, individuals who can be challenging without being combative or obstructionist. As long as these qualities are satisfied, it matters little whether or not these individuals support the use of animals in research or are simply resigned to the inevitability of such research.<sup>5</sup>

Why should research facilities buck the current trend by appointing to their IACUCs individuals known for their work on behalf of animals? There are a number of overlapping reasons:

- to follow the spirit of the AWA
- to gain advice not only from a different (non-institutional) perspective, but from a statutorily relevant perspective (animal welfare)
- to enable at least one person on the IACUC to see his/her role exclusively as an advocate for the research animals
- to be discouraged from undertaking proposed projects that would stretch the limits of public acceptance
- to demonstrate a willingness to be open to outside scrutiny
- to engender good community relations
- to educate animal advocates about the research process
- to lessen the polarization between the animal research and animal protection communities

## **POTENTIAL PITFALLS**

We recognize that many supporters of animal research are likely to see potential for more harm than good from appointing animal protectionists to IACUCs. In this section, we identify and address several counterarguments to the current proposal.

- *"All we'll gain are ideological, combative, naysayers who will disrupt our meetings"*

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<sup>5</sup>Individuals who fit this overall profile and are considering service as an NAM should themselves deliberate carefully. Some of the animal advocates who have served as NAMs have described their experience using words such as "miserable," "anguish," and "stressful" (15). Individuals should think twice before putting themselves in a situation in which they are going to experience such emotions.

One of the roles of NAMs is to raise questions about the care and use of animals that otherwise might not arise during committee deliberations. If this is done in a consistently disruptive manner, then the offending individual should be replaced, as should any member who prevents the committee from carrying out its mandated functions. Fortunately, this situation should be precluded by careful selection of NAMs.

- *"Open, frank discussion will be stymied by the presence of individuals with ties to the animal protection community"*

This may be true initially but should subside with time, as NAMs demonstrate their commitment to working within the IACUC system. Case histories have already borne this out (6).

- *"Meetings will bog down in ceaseless probing of animal welfare minutiae"*

We believe that NAMs will quickly learn what the key issues are and concentrate on these, rather than on less salient features of protocols.

- *"Animal protectionists will leak confidential information and pose a security risk"*

Any IACUC member could use information gained from committee service to bring unwelcome scrutiny to an institution, and we recognize that this concern would be particularly applicable to NAMs who were animal advocates. However, this is another situation that should be precluded by careful screening of NAM candidates. In addition, NAMs probably are a minimal security risk given that they typically do not have unrestricted access to animal quarters. Moreover, concern over IACUC members leaking trade secrets is largely misplaced given that this activity is illegal under the AWA and that there is no need to put such secrets in protocols.

- *"Some institutions have tried this in the past and it hasn't worked out"*

Although research facilities typically have not appointed animal protectionists to IACUCs, they have occasionally done so. There have been isolated cases in which animal activists have been appointed to IACUCs only to be dismissed or to resign after relations become strained (4). The reasons behind these occurrences differ from case to case. On the other hand, there have been other cases of such arrangements proving to be practical and productive (6).

- *"Even if this person works out well, he/she is likely to be pestered by animal rights crazies"*

Community representatives serving on IACUCs should be willing to communicate with any member of the community who has concerns about the care and treatment of the animals at the facility in question. Individuals who feel they don't have the time or patience to be a true community representative should not seek appointment as a NAM.

An additional counterargument to our proposal may be advanced by critics unfamiliar with IACUCs in practice, namely, that animal protectionists will prevent meritorious research from being approved. Most IACUCs operate on a simple majority vote; when this is the case, no one person can block a proposal.

In light of the nature of the potential problems, we conclude that facilities face little risk if they exercise common-sense precautions in implementing the current proposal.

## CONCLUDING REMARKS

Our proposal for animal protectionists to be appointed to IACUCs is consistent with a community relations function that many IACUC chairpersons apparently envision for their NAMs. In Orleans' survey of IACUC chairpersons, mentioned above, a "good many mentioned that the



community member's presence was to provide assurance to the community that all animal experiments were appropriate and necessary and deserved community endorsement" (6, p. 113). Surely, however, the mere existence of the NAM slot on IACUCs is not enough to provide a meaningful assurance. Rather, such assurances would be more credible if the NAMs had a history of animal advocacy and if they served openly as a liaison between the facility and the community.

We have argued above that our proposal is consistent with, but not mandated by, national policy in the United States. However, national policies in Germany, Denmark, and Switzerland explicitly call for representation from animal welfare groups on regional or national committees that oversee animal experimentation (6). Moreover, Australian policy calls for at least one person who is an animal welfarist to serve on that country's equivalent of IACUCs; the official description of that member parallels the current proposal almost exactly:

A person with demonstrable commitment to, and established experience in, furthering the welfare of animals, who is not employed by or otherwise associated with the institution, and who is not involved in the care and use of animals for scientific purposes. The person should where possible be selected on the basis of membership of an animal welfare organization....(3)

This policy has reportedly caused no major difficulties (8).

What is the likely impact of facilities implementing the current proposal? Orlans' informal survey of 16 former NAMs, all of whom were animal advocates, provides some measure of the limited but important effect (6). She concluded:

They [the animal protectionist NAMs] must be satisfied with having only moderate or minor impact on the committee and seeing only occasional disapprovals of protocols. Their overall impact of contributing balance and some measure of public accountability to the proceedings must suffice (p.111). A commonly stated opinion among the survey respondents was that the value of being a community member lies not so much in the specific reforms effected but in being a constant reminder to the institution of the outside world (p. 112).

HSUS board member Robert Welborn reported that his own IACUC experience was emotionally trying, but he felt it was nonetheless important for animal protectionists to seek appointment to IACUCs and to work within the system (14, 15).

Institutions that decide to appoint local animal protectionists to their IACUCs face the task of identifying suitable candidates. The HSUS stands ready to help. Indeed, The HSUS has already contacted a number of universities throughout the country, offering our assistance. Other potential sources of help include local, regional, or national humane societies/animal protection organizations, as well as campus-based organizations, which may know of suitable non-affiliated candidates.

In conclusion, we encourage research institutions to appoint local animal protectionists to their IACUCs and to have these individuals serve as a liaison to the community on matters relating to the institutions' care and treatment of animals in research. We believe such individuals, when carefully chosen, offer a number of advantages and pose little risk.

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# The Role of the Librarian in the Work of the Institutional Animal Care and Use Committee

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This article originally appeared in *Animal Welfare Information Center Newsletter* 6(2-4): 9-11, Winter 1995/1996. The article may be found at <http://www.nal.usda.gov/awic/newsletters/v6n2/6n2keefe.htm>

The Animal Welfare Act of 1985 resulted in the establishment of the IACUC to review all research protocols involving the use of animals, inspect the institution's animal facilities every 6 months, ensure that all personnel working with animals are properly trained in the care and use of the animals, respond to any reports of improper treatment of animals, and act as the conscience of the institution in the care of its laboratory animals.

## THE INFORMATION NEEDS OF THE IACUC

The members of IACUC and those using animals in education, testing and research need to be made aware of the Animal Welfare Act of 1985 and the guidelines for the care and use of animals in these activities provided in the Code of Federal Regulations (9 CFR Chapter 1). They need to know how to access printed and online bibliographies on topics such as the care and use of specific species in the laboratory, animal models in biomedical research, the alleviation of pain in animals used in the laboratory, and the use of alternatives in research using animals. The librarian can provide the following information services to meet these needs:

1. Maintenance of a file of resources:
  - a. National Agricultural Library (NAL) and National Library of Medicine (NLM) publications on animal welfare and use of animals in the laboratory (see appendix).
  - b. Newsletters from animal welfare organizations such as Scientists Center for Animal Welfare (SCAW) and Center for Alternatives to Animal Testing (CATT) (see appendix).
2. Provision of database searching service to allow principle investigators opportunities to provide assurances that their research does not duplicate work already done, and that their procedures are carried out with a minimum of discomfort to the animals. This service is also necessary for investigators to determine if there are alternative species lower on the evolutionary scale that could be used in the research or if *in vitro* methods could be used instead of *in vivo* methods.
3. Promotion of information available on animal welfare publications, audiovisuals, Internet resources, and database searching tips in the publications of the institution the librarian serves, such as the library newsletter or the Department of Animal Resources newsletter.

## DEVELOPMENT OF LIBRARY SERVICES FOR THE IACUC AT EMORY UNIVERSITY

In 1987, the chair of the Institutional Animal Care and Use Committee (IACUC) at Emory university requested that a librarian on the Health Sciences Center Library (HSCL) staff be appointed as liaison for the IACUC. I was assigned that role and it has been a very challenging and rewarding experience. The first task was to check the bibliographies in the "Guide for the Care and Use of Laboratory Animals" published by the National Institute of Health (NIH) against Emory University Libraries holdings. Items not owned were checked by the chair of the IACUC to submit for purchase with the understanding that some items might not be purchased but obtained, if needed, through interlibrary loan.

In 1988, the IACUC sent me to the Animal Welfare Information Center (AWIC) located in the NAL, and to the Office of Veterinary Affairs at the NLM, to acquaint me with the resources available on animal welfare and the use of laboratory animals in biomedical research. Using the resulting lists of resources and contact persons for information on animal welfare, I prepared a brochure to send to Emory personnel working with animals announcing that in response to the



Animal Welfare Act of 1985 and the mandates published in the Code of Federal Regulations (9 CFR Chapter 1), the HSCL had assessed the Emory University collection and was prepared to support their information needs. Emphasis was placed on available databases that would help them provide the assurances requested by NIH that they were not unnecessarily duplicating research and that they had searched the literature for possible alternatives to both the animals being used and the procedures applied to the animals.

In 1991, Jean Larson at the Animal Welfare Information Center was contacted to plan for an AWIC workshop at Emory. IACUC members, researchers and librarians at Emory were invited and assembled in the HSCL classroom for a half-day session. The thrust of the presentation was the "3Rs" of Russell and Burch--reduce, refine, and replace--and the importance of assurances by principal investigators that they have searched the literature to determine if they can apply one or more of the "three Rs" to their research. Multi-database searching was stressed as the way to provide these assurances. The workshop was a great success in raising awareness among the three groups of people that attended. Shortly thereafter, I received an invitation to be an ex-officio member of the IACUC. In 1992, I was invited to become a voting member of the IACUC and pursue these activities along with additional duties such as reviewing applications for the IACUC's monthly protocol review meeting and participating in the animal facilities inspection every six months.

## **LABORATORY ANIMAL CARE AND USE TRAINING AND THE EMORY INFORMATION INFRASTRUCTURE**

Another responsibility of the IACUC is to document that personnel working with animals at their institution have received training in the care and use of the animals with which they are working. A committee consisting of the IACUC chair, the University Veterinarian, the head of the HSCL Media Services, and myself, decided upon a test for certification. This certification at Emory is given upon completion of an audiovisual/computerized test produced by the Laboratory Animal Training Association (LATA). The LATA program best suited our need to provide training to over 900 people working with animals at Emory and utilize our new developing information infrastructure. Our ultimate goal is to provide access to the video training tapes via a campus cable station accessible to personnel at Emory vivarium locations all over Atlanta. Unfortunately, off-campus sites do not yet have the cable access needed and are being served by scheduling the tapes for group viewings at their departments or in the library. By the time we received our tapes, the deadline for certification was very close and several hundred people requested access within a short period of time, which became a real challenge to the staff in Media Services.

The ultimate goal for access to the computerized test is for individuals to be able to access the library server via MS-DOS and Ethernet on their PCs. However, remote locations are not on Ethernet and some sites on campus cannot get into the server because of the security system protecting patient records at Emory Hospital and Clinic. Happily, another route was found for those unable to access the computerized test by using a modem to dial in with PC Anywhere. We also have stations in HSCL Media Services for those without remote computer access.

The LATA software for the tests provides a report system that lists names of participants, their department, the titles of tests they took and their grades. In all there are nine training videotapes to view, depending on the person's animal care activities, with tests for five of these tapes (see appendix). The chair of IACUC can view these results, sorting out those with grades below 60 to be notified to repeat the test, and then print out the report to send to LATA. LATA then provides certificates for each of the five tests that were successfully completed, charging the IACUC \$3.00 per test taken and \$3.00 per certificate prepared and mailed.

Needless to say the job of trying to clarify these access problems to the over 900 Emory people has been a challenging one and we report on this in hopes that it will alert others to possible pitfalls. The HSCL Media Services staff should get a special award for juggling electronic resources to provide access as fast as they could for the onslaught. The IACUC chair and his secretary have valiantly dealt with the monthly reports, scores, certificates and queries that have added to their busy agenda of dealing with IACUC applications and myriads of animal welfare-related issues and requests.



## CONCERNS OF A LIBRARIAN ON THE IACUC

My role as IACUC member has taken me beyond my library concerns and into a world of ethical decision making that the IACUC deals with at monthly meetings with vigor and care. There are 20 members of the Emory IACUC: six veterinarians, two veterinary interns, one clergy, the director of the Atlanta Humane Society, the director of the Office of Sponsored Programs, nine faculty/research members, and myself acting as the lay representative on the committee as well as liaison for the HSCL. Our members span the Yerkes Primate Center, the Veterans Administration Medical Center as well as the Emory campus departments. This allows an excellent array of expertise with which to review the varied applications the IACUC receives. It has been gratifying to me, as one of the lay representatives, to see the committee's great concern that the applicants' presentations of their reasons for doing their project and their descriptions of the procedures that will be used on the animals are given in lay terms as requested by NIH. Of key importance is their careful monitoring of the assurances, required in CFR 9 sec 2.31d, that alternative models are not available and that the research does not unnecessarily duplicate previous work. The methods and sources used to determine this are provided, and any database(s) searched are listed with date of last search attached. My main duty as lay representative is to question any shortcomings in the foregoing concerns and any other discrepancies I might spot in a protocol. As a librarian, my main duty is to provide information to the committee and to the applicants about databases and resources that might shed further light on an area of research or testing.

## APPENDIX

### RESOURCE FILE

#### 1. NAL publications

##### a. Bibliographies

QB series (Quick Bibliography Series)  
SRB series (Special Reference Briefs)  
AWIC Series (Animal Welfare Information Center)  
STS series (Search tip Series)

##### b. Newsletters

*Animal Welfare Information Center Newsletter*  
Contains animal welfare and IACUC information.

#### 2. NLM publications

##### a. NLM Current Bibliographies in Medicine

##### b. SBS Specialized Bibliography Series

These can be found in the monthly issues of Index Medicus

#### 3. Animal Welfare organizations' newsletters

##### a. Scientists Center for Animal Welfare (SCAW) Newsletter

##### b. The Johns Hopkins Center for Alternatives to Animal Testing (CAAT)

#### 4. Key Databases that cover animal care and research involving the use of animals

AGRICOLA

BIOSIS PREVIEWS

CAB ABSTRACTS

EMBASE

FEDERAL RESEARCH IN PROGRESS

LIFESCIENCES

MEDLINE

PSYCHINFO

TOXLINE

TOXNET  
ZOOLOGICAL RECORD

**5. Animal welfare organizations**

AWIC Animal Welfare Information Center  
National Agricultural Library, USDA  
10301 Baltimore Boulevard  
Beltsville, MD 20705-2351

SCAW Scientists Center for Animal Welfare  
Golden Triangle Building One  
7833 Walker Drive Suite #410  
Greenbelt, MD 20770

CAAT The Johns Hopkins Center for Alternatives to Animal Testing  
The Johns Hopkins School of Hygiene and Public Health  
615 N. Wolfe St  
Baltimore, MD 21205

**6. LATA Integrated Training Program**

Laboratory Animal Training Program (LATA)  
54 Remington Dr Suite 301  
Highland Village, TX 75067

Tape #1 The New Research Environment  
Tape #2 The New Research Environment  
Tape #3 The Humane Care and Use of Laboratory Animals (TEST AVAILABLE)  
Tape #4 The Humane Care and Use of the Mouse, Rat, and Hamster (TEST AVAILABLE)  
Tape #5 The Human Care and Use of the Rabbit and Guinea Pig (TEST AVAILABLE)  
Tape #6 The Humane Care and Use of the Dog and Cat (TEST AVAILABLE)  
Tape #7 The Humane Care and Use of Nonhuman Primates (TEST AVAILABLE)  
Tape #8 Aseptic Surgery of Rodents  
Tape #9 Anesthesia and Analgesia of Rodents

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**See also USDA Animal Care Policy 15–IACUC  
Membership—in the section U.S. Government  
Principles, Regulations, Policies, and Guidelines**



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## Useful World Wide Web Site

**The University of Arizona Institutional Animal Care and Use Committee Handbook**

<http://www.ahsc.arizona.edu/uac/iacuc/member.shtml>

The University of Arizona IACUC maintains at least 3 Community Representative membership positions. This page details the role of the IACUC community members.

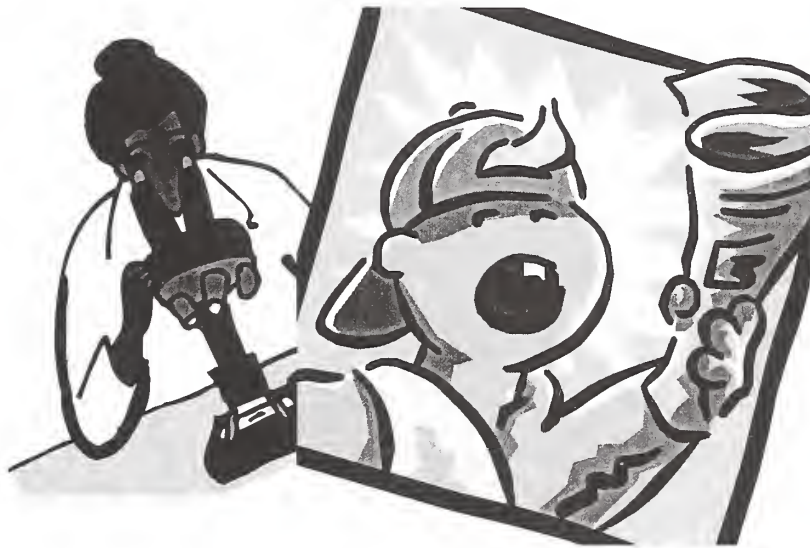
**The University of Tennessee Institutional Animal Care and Use Committee**

<http://www.ra.utk.edu/ora/labaniml/UTBYLAW6.html>

IACUC Membership- a very complete description of the composition, officers and their responsibilities, terms and appointments, and member responsibilities.



# Investigator Issues and Public Viewpoints







# Trapped in a Guilt Cage

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I began entering laboratories in 1985 as an anthropologist might study villages in other cultures. I would hang out and become almost a native for weeks and sometimes months at a time, so I could describe the culture of biomedical research. I watched how researchers behaved with animals and with each other, and asked questions about their work in everyday conversations and more formal interviews. In some cases, I was even permitted to do some of the work of technicians and caretakers, from cleaning cages to carrying out experiments. So far, I have studied 15 laboratories and research centers with around 400 principal investigators, veterinarians, postdoctoral and graduate students, research technicians, and animal caretakers.

What prompted me to conduct this fieldwork was the controversy over the propriety of animal research. While this rapidly intensifying debate has led to greater regulation of the use of animals in the laboratory, it struck me that little if any attention has been paid to the impact of experiments on the people who carry them out. It would be naive to think that researchers might not experience some conflict over using animals in experiments.

While most people I studied seemed to have come to terms with their use of animals, many had not. Few people had frequent signs of depression or anxiety, such as nightmares, sleep loss, and increased alcohol consumption, that they attributed to working with animals. However, more moderate and episodic feelings of discomfort were common and were expressed as background uneasiness and guilt. About 20 percent of the interviewees, for instance, compared animal experimentation, however tentatively, to the Holocaust. Uneasiness was particularly noticeable among newcomers; with seasoned workers, it was most common among animal caretakers. It existed among technicians, and was relatively rare among veterinarians and scientists. How did researchers live with whatever uneasiness they felt?

## Troublesome Emotions Denied

Open discussion of these feelings was taboo. Scientists, veterinarians, and administrators tended to deny that laboratory workers could be troubled by their use of animals. Uneasiness was not seen as an issue, and was not allowed to intrude on the normal course of work. This attitude was made apparent to me in a firsthand way. Invited to speak at a conference of animal researchers, I chose to call my talk, "The Experimenter's Guilt." I was told that my choice was too controversial and that "Stress Among Researchers" would be more palatable. A popular journal about laboratory research invited me to publish this talk, but insisted that the term "stress" was too extreme and inaccurate. They preferred the term "uneasiness," which I used.

Soon after its publication, I was asked to speak on this subject to the staff at the research center of a major pharmaceutical company. I was told, however, that I could not use "uneasiness" in the title because it would inflame research directors. They suggested "How Researchers Deal with Their Feelings." To make matters easier, I have decided simply to call future talks "Untitled."

New workers believed they were not supposed to talk about their feelings to anyone. Feelings remained private, extraneous to the "real work" of the laboratory. Individuals believed that their colleagues were better able to handle their feelings, only vaguely aware that many others dealt with the problem in similar ways. Yet within the laboratory culture were unspoken rules and

resources for dealing with unwanted emotions and thoughts, despite the silence surrounding this topic.

People most commonly coped by seeing laboratory animals as different from pets, zoo animals, or wild animals. Once the creature was defined as a laboratory animal, certain emotions would not be tapped, making it easier to carry out experiments. Many social forces in the laboratory culture helped to make this definition. Animals became “models” chosen to suit particular experiments. Their cost was listed under “supplies” in grant proposals, and they could be ordered through catalogues of animals specially bred for laboratory use.

## **Turning Animals Into Objects**

As interchangeable and anonymous objects, each animal or an entire cage was identified by a code that might include the date of delivery, the researcher's name, the experiment's number, and the animal's number. These codes were clearly displayed on all cages, and the identification numbers of some animals were marked on their bodies: the ears of mice were hole-punched and the bellies of dogs and primates were tattooed. Unstated rules dictated how people interacted with laboratory animals. Social norms stipulated that they were objects and not pets, and sanctions supported this definition. For example, the chief technician in one laboratory had to tell a worker to stop naming sheep because that made it harder for others to perform the experiments.

Making this definition was easier for researchers than it was for technicians and caretakers. Having taken laboratory courses that used animals in college or medical school, many researchers learned not to make laboratory animals into pets long before starting their first full-time research positions. Instead, animals were transformed into data or silent research collaborators. Lack of direct contact with the animals reinforced the transformation. Researchers, typically, did not routinely conduct experiments and handle animals; they stopped by their laboratories for a brief visit during the day or occasionally performed delicate surgery on animals after they were fully anesthetized. Also, most applied biomedical researchers were primarily interested in answering particular scientific questions, and animal models would be selected on that basis.

Technicians and caretakers found it harder to treat animals as objects because they commonly lacked prior research experience and had frequent and direct contact with the animals. They would learn not to treat them as pets after being shocked by the death of a special animal that they regarded as a friend or partner. While people tried to detach themselves from the animals, they rarely succeeded completely. Some described themselves as “a little desensitized.” In the words of one technician: “You have to put up some walls. Sometimes you have to create a distance between yourself and the animal you are working with. But I try occasionally to do some checking to see how big that distance is. I don't want it to become so big that I lose the sense that I'm working with animals.”

While most people accepted this detachment as necessary for self-protection, not everyone found it comfortable. One technician, for instance, told me that “it didn't feel right” to stop playing with the primates in her laboratory. But those who did bond closely to laboratory animals were often reminded and even teased about the dangers. At one facility, for example, a technician was called a “problem child” by her peers for this reason. At another facility, in an effort to curtail bonding, a scientist told his technicians to remove the names of animals from cage identification cards because it “looked unprofessional.”

Workers still found ways to treat animals as pets and express their affection for them. Technicians and caretakers would single out an animal for a laboratory pet. Often a mouse, rat, or guinea pig, these animals were not experimented upon or at least not sacrificed. In addition to being named, caged singly, fed special foods, and given much attention, they would also sometimes be taught tricks and allowed occasionally to run free in the laboratory. They were safe animals with whom workers could become attached without fear of loss. Affection for animals also resulted in “rescues” where they were taken home by workers who were strongly attached to them. For instance, in all seven dog laboratories studied, staff members had quietly taken home at least one animal in the previous year. And photographs, cartoons, dolls, and other images of animals hung on the walls of



laboratories, as constant reminders to workers that they cared about animals and found them interesting.

It was also important for people to learn to cope with the death of animals. Novices were usually eased and coached into killing their first animals. Sometimes long before they did their own killing, they observed others doing it matter-of-factly. More experienced people almost never cajoled or pushed newcomers to kill and waited until they seemed ready to do it. Still, certain types of sacrifice were contrary to the novice's "instincts," such as slamming rodents against the bench or cutting off their heads, and this required special teaching. Newcomers were reassured that, if done correctly, the death was quick and painless, regardless of the particular method they used. For example, after breaking the necks of mice, new workers were often troubled by animal movements that looked like suffering. Someone more senior would usually explain to the novices that these movements were only "muscle spasms."

### **Rituals Help Workers To Cope**

For some people, it was important not to see death as just another task in the day because it would quickly become mechanical, especially in laboratories that conducted experiments like factory assembly lines where the individuality of animals was lost. As one researcher said, "It doesn't mean that we're callous about killing them, but there's not really a second thought for that animal as an individual." Death could become merely the final step in the protocol, signifying noxious tasks such as disposing of corpses and more pleasant associations such as going home for the day. In a few laboratories, workers followed certain rituals when killing animals, giving death special meaning. In one case, the scientist asked her graduate students and technicians to observe a minute of silence before sacrificing animals. In another laboratory, a technician privately recited a prayer each time she killed an animal, asking that its death be forgiven. Some laboratories made memorials to commemorate "favorite" animals that died.

Yet for most people, using the term "sacrifice" was the primary device for giving meaning to death. Journals and grant agencies prohibit use of this term, and some individuals described it as an inappropriate euphemism, but it did indeed mean something special to many research workers. "'Killing' connotes no purpose, while 'sacrifice' connotes there is a reason," noted one technician. Similarly, an investigator explained to me that "sacrifice" was different from "wanton murder" described in detective novels; the former had a larger, worthwhile aim while the last was pointless. Besides "sacrifice," there were other terms with less meaning that shielded people from the harshness of death. Animals were "dispatched," "terminated," "cervically dislocated," "exsanguinated," "decapitated," or "put down," while whole rooms were "depopulated" or simply "cleaned."

People also acquired a vocabulary that aggressively framed their actions toward animals, reinforcing the image of animals as objects. People injecting animals were shooters and their injections were "sticks." "Guns" were syringes attached to devices like pool cues that reached into cages, and "torture chambers" were devices to restrain mice. Animals were labeled according to their experimental purpose: there were "controls," "recipients," "donors," "carriers," "bleeders," "breeders," "junk," or simply "X-animals." Even the very term "experiment" was infrequently used; people more often referred to a "preparation" or "project." And the subjective term "suffering" was deliberately avoided in favor of the more neutral "distress."

### **The Scientist As 'Hunter'**

Rationalizing the use of animals in science was also a mainstay in the coping skills of researchers. People in laboratories saw little difference between animals used in experiments and those killed for food and clothing. A few compared it to hunting, which they saw as acceptable if animals were eaten rather than killed merely for recreation. As one researcher said of his hunting: "I do it strictly for the meat from the rabbits, to pheasants, to ducks, to geese. I've had opportunities to shoot bear, but I haven't because bear meat isn't good to eat and I can't see killing something that I can't use personally." I was frequently reminded that most laboratory animals were bred for research, so they knew of no other existence. And when former pets and strays were obtained from shelters



where they would have been killed “wastefully,” their use in experiments was seen as giving the animal's life and death added purpose.

For the most part, though, people did not have elaborate moral justifications for their use of animals. Instead, many of them appeared ethically inarticulate. Predictably, scientists and research technicians saw scientific and medical goals as moral imperatives to do their work. Caretakers justified their work with animals by ensuring that they could not be better treated, giving the animals enough love and attention in their last days so they could experience what it was like to be loved as pets. For some workers this was almost an addiction. People spoke about being unable to quit because they were afraid that no one else could be hired that would be as dedicated as they were to the welfare of laboratory animals.

I also observed a different way of coping among those who felt “animal activists” seriously threatened biomedical research. Some scientists have started a countermovement to educate the public about the need to use animals in science. Part of this campaign has been to denounce activists as dangerous and evil because medical advances would halt if they succeeded in preventing animal experiments. By demonizing those strongly opposed to animal research, the charge of immorality leveled at researchers was reversed.

Finally, researchers had to learn to manage the occasional sarcastic remark, heated argument, or blunt criticism encountered when discussing their work with lay people. New workers were often disturbed to be called “mouse murderers” and discovered that conversations about animal experimentation quickly degenerated into a “ping pong” of polarized opinions. Scientists, though, were less likely than technicians or caretakers to be put in this position because as physicians or academics they could talk about their work without mentioning animal experimentation. Also, their social networks usually included many people sympathetic to biomedical research. Those not in this position would sometimes, out of frustration, carefully avoid mentioning animal experimentation by telling people that they “did cancer research” or “worked at Boston General Hospital.” Others would assess whether conversations were likely to become “shouting matches,” gradually releasing more information about their use of animals as long as the unfolding talk seemed safe to them. Some also told people that they owned pets themselves, perhaps to suggest that they were hardly insensitive and heartless scientists.

While these coping devices certainly made it easier for many people to conduct experiments on animals, it is not clear whether these adjustments should be encouraged. There are two lines of thinking. Some people argue that by coping in this manner, there will be an ethical blunting or a coarsening of the moral sensitivities of researchers. Others are more struck by the significance of the conflicts that prompt defensive behavior. The surfacing of these conflicts among researchers may be due to the diffusion into the laboratory of society's heightened awareness of how animals should be viewed and treated. Coping devices will be called out when humanity's standards clash with traditional scientific practice. This is cheering to some who see this as a willingness to pay more attention to humanitarian ideals in animal experimentation.

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AB- The practice of biological science has changed dramatically since mid-century, reshaped not only by a rapid series of landmark discoveries, but also by governmental directives, institutional policies, and public attitudes. Until 1964, the major influences were the mentor, who provided direction and indoctrination into the culture of science, and in dentistry, the newly established NIDR, which fueled the research engine with an expanding research and training program. The 1965-74 period witnessed the advent of the Institutional Review Board, an increased social involvement of biological scientists, and a recognition of the need for biological and physical safeguards in the conduct of research. The most turbulent years were 1975-89, when there was a confluence of animal rights activism and regulation, growing concerns with scientific fraud and publication malpractice, and the stresses and strains (and opportunities) resulting from the rapid expansion of the academic-industrial complex. The current period is characterized by rapid pace, high volume, and an increased depth and breadth of knowledge-a major change in scale in the conduct of science. It is an exciting time but one in which ethical issues are multiplying. Attention must be paid.  
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## Useful World Wide Web Sites

### Instructions for Principal Investigators

<http://www.fsu.edu/~FSULAR/framea.html>

This site is provided by the Florida State University Laboratory Animal Program.

### Responsibilities: Investigator

<http://www.unl.edu/research/ReComp/IACUC/invrespb.htm>

This site is provided by the University of Nebraska at Lincoln Institutional Animal Care and Use Committee.

**U.S. Department of Agriculture, Animal and Plant Health Inspection Service**

<http://comments.aphis.usda.gov/>

Viewers are able to comment on an open proposal or read comments made by the public on proposed USDA rules or regulations.





# Alternatives and Database Searching





# IACUCs and AWIC

## The Search for Alternatives

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*[Mention of commercial enterprises or brand names does not constitute endorsement or imply preference by the U.S. Department of Agriculture. The views expressed by the authors do not necessarily represent positions or policies of the U.S. Department of Agriculture or any agency thereof and should not be interpreted as such.]*

"Do we see some veterinarians still pursuing the methods of the ancients and perpetrating pain on a helpless subject... The result has been, and the feeling still exists, largely among the laity, that we are a hard-hearted profession..."

A modern day diatribe by animal activists. Not really. Those words were written by Dr. J.P. Turner in the Proceedings of the American Veterinary Medical Association in 1899. He was lamenting the fact that many of his colleagues were resisting the use of anesthetics to restrain animals during surgery in favor of hobbles and rope tie-downs, "the accustomed way, or the methods we were taught." While things have certainly changed, it is still not uncommon to hear "that's the way we've always done things." However, with the passage of the Improved Standards for Laboratory Animals Act in 1985, Congress let it be known that it is concerned about the use of animals in painful procedures. Under this law, scientists performing painful experiments on animals must document if there are alternative methods to the painful procedure and report this information to the Institutional Animal Care and Use Committee (IACUC) when they submit their animal use protocol form for approval. It is then the responsibility of the IACUC to determine if the alternative methods should be used. To assist IACUCs and investigators in complying with this portion of the law, Congress established the Animal Welfare Information Center (AWIC) at the National Agricultural Library. In the next few pages, we will look at the critical role that IACUC's play in the animal use approval process, especially the problems associated with documenting whether or not alternatives exist, and how AWIC can assist members of an IACUC and/or scientists.

The U.S. Department of Agriculture views alternatives with an eye to the 3R's concept so eloquently described by W.M.S. Russell and R.L. Burch in *The Principles of Humane Experimental Technique*--reduction of animal numbers, refined procedures to minimize or avoid pain, and replacement of animals with non-animal models. According to the Animal Welfare Act (AWA) regulations (9 CFR § 2.31(d)), "the IACUC shall determine that the principle investigator has considered alternatives to procedures that may cause more than slight pain or distress to the animals, and has provided a written narrative of the methods and sources used to determine that alternatives were not available." The IACUC is also responsible for ensuring that the proposed research does not unnecessarily duplicate other research. Along with several other items, AWIC considers these the information requirements of the act (the other sections being scientific justification for withholding anesthetics or analgesics, or using animals in more than one major operative procedure from which s/he is allowed to recover).

While the regulations seem fairly straight forward, it has been our observation that many people are unsure exactly what an alternative is and are confused as to what information is required to show compliance. There are many opportunities to incorporate alternatives into an experimental procedure; however, many IACUCs and scientists mistakenly assume that only non-animal methods satisfy the definition of an alternative. Although outside the scope of this paper, some alternatives might include pair-housing of rodents to alleviate the distress of isolation, proper use of analgesics in a post-procedural period, or reducing the volume of a receptor binding assay thereby reducing the amount of animal tissue needed to quantify the reaction and ultimately reducing the number of



animals. The point is that IACUC's and investigators need to fully understand that identifying viable alternatives requires more than looking for non-animal models.

Animal welfare regulations require, as a minimum, that an investigator perform a search of the literature in an attempt to identify alternatives to painful procedures. Cynthia Smith, an AWIC staff member, wrote a method paper on searching for alternatives that is an excellent overview of this type of searching. But what is important to realize is that a multidatabase approach is necessary, as an alternative procedure or method may come from outside the specific discipline being studied. For example, if you concentrate on mammalian models for studying Parkinson's disease or diabetes, emerging fish models may be overlooked.

It is also important to conduct the literature search on a case by case basis. AWIC staff often are asked by an IACUC to perform a literature search on a painful procedure outside of the context of an experiment. It is impossible to look for alternatives to something as general as thoracotomies in dogs. Some of the questions that need to be addressed are why is the procedure being performed? What is the expected outcome? Is the procedure terminal? Only with complete information can a search be performed, and the IACUC properly evaluate the literature search.

Some IACUC's require attaching a literature search to the protocol with a list of the databases and strategy used to show that a good-faith effort was made to find alternatives. Many others require only that a box be checked indicating that alternatives are not available or may simply ask for a few key words and the database searched. Still others list AWIC as a source of information on the protocol form leading to many requests for information. Regardless of the system used all are fraught with problems. When an investigator contacts AWIC for help in completing an alternatives search, we commonly ask them to fax a copy of the protocol to us so that we will have all pertinent experimental information at hand. It is not uncommon to find the statement "AWIC was consulted and no alternatives were found" typed onto the protocol sheet that we are seeing for the first time. Oftentimes it is plain to see that the alternatives search is clearly an afterthought, being performed simply to comply with the law. The most common refrain is, "I'm turning in my protocol tomorrow, and I see that I have to have a literature search, can you fax that to me?" In our roles as members of Federal IACUC's, we routinely see protocol forms filled out stating that a literature search was performed, but, when we ask the investigator to provide us with a copy of the search, it usually has not been conducted. In other cases, the entire concept of alternatives is simply ignored by both the IACUC and the investigator. Are these examples the norm? Maybe not, but they occur often enough that there clearly is a problem with IACUC oversight of this particular part of the regulations. Comments made to us at meetings or workshops reveal that many scientists and IACUC members view the alternatives search as unnecessary government intrusion into the research process, and not as a resource that might enhance or improve their research. Not surprisingly, a Department of Agriculture report on enforcement of the AWA by the Animal and Plant Health Inspection Service, Regulatory Enforcement and Animal Care (ed. note: this unit is now called Animal Care), found that IACUC's do not always meet the standards of the act and that this is attributable to the fact that committee members are not always aware of the act's requirements. Two of the major deficiencies noted are failure to properly address the use of alternatives and failure to provide written assurance that activities are not unnecessarily duplicative.

With these problems fresh in mind, what can or does AWIC do to help animal care committees comply with the law? AWIC was established to provide information pertinent to employee training, to prevent unintended duplication of animal experimentation, to reduce or replace animals used in painful experimentation, or on refined methods to minimize pain to animals when no other model can be found. To help IACUC's, investigators, and animal research support people understand the alternatives section of the regulations, AWIC staff developed a two-day workshop called "Meeting the Information Requirements of the Animal Welfare Act." The workshop provides an overview of the Animal Welfare Act looking specifically at the information requirements, Federally mandated IACUC functions, criteria for granting IACUC approval for animal research, and the required contents for an institutional training program. A representative from the U.S. Department of Agriculture's REAC staff is also available for a question and answer period. The workshop also provides an overview of the "alternatives concept," multiple database

resources, concepts involved in developing search strategies (but no magic formulas), and, finally, the opportunity to gain hands-on searching experience using the DIALOG database system.

The success of the workshop is measured not only by the fact that every class held at the National Agricultural Library is booked months in advance but also by the number of requests we receive to bring the workshop to offsite facilities. Even more importantly, however, are the comments received from people who have taken the training class. The most common sentiment is that the class should be required for all members of IACUC's as it addresses many of the problems common to successful IACUC functioning.

If it is true as Ben Franklin said that an investment in knowledge pays the best interest, then perhaps AWIC's greatest utility to the scientific community is the capability of providing comprehensive literature searches or other information on alternatives, animal husbandry, animal models, philosophical issues, and many other topics related to animal research. When AWIC is requested by an IACUC or an investigator to perform a literature search, the package of information they receive includes the search strategy, the databases searched, and the literature information that documents whether alternatives are available and if the research is duplicative. We may also include a copy of one or two pertinent articles. Many IACUC's, working through institutional libraries, also maintain collections of bibliographies produced by AWIC on topics from anesthesia and analgesia to zoonoses. The AWIC staff also produces a newsletter that covers topics such as environmental enrichment, IACUC communications, alternatives, etc.

How is AWIC able to provide such a breadth of information to such a diverse audience? We owe this ability to a much underutilized resource, the National Agricultural Library (NAL), as well as new technology such as the World Wide Web, and the numerous databases available through services such as DIALOG. The NAL houses one of the largest collections of veterinary literature in the world, and is developing one of the most comprehensive collections of laboratory animal literature. These materials include NAL's AGRICOLA database, more than 400 videos and slide programs that can be used in institutional training programs, most relevant journals, codes of practice, newsletters, texts, and other published materials such as conference proceedings and abstracts relating to laboratory animals and farm animals used in biomedical research. Because of international exchange agreements, AWIC and NAL also work closely with other agencies providing information or regulatory oversight to animal care committees throughout the world. In this way, we are able to bring a broader perspective to many issues.

In 1996, AWIC is celebrating its 10th anniversary. In its brief existence, AWIC and NAL have worked hard to develop a comprehensive resource to assist IACUC's in carrying out their enormous responsibilities. Animal care committees face many problems in assuring that their institutions are complying with the Animal Welfare Act and the Animal Welfare Information Center is available to help them.

For additional information contact the staff at: Animal Welfare Information Center, U.S. Department of Agriculture, Agricultural Research Service, National Agricultural Library, 10301 Baltimore Avenue, Beltsville, MD USA 20705-2351, Tel: (301) 504-6212, Fax: (301) 504-7125, e-mail: [awic@nal.usda.gov](mailto:awic@nal.usda.gov), WWW: <http://www.nal.usda.gov/awic>

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# The Alternatives Concept

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The growth of scientific interest in the topic of alternatives has been marked by legislative initiatives and campaigns by animal advocates against animal testing. However, the topic is also marked by rhetoric that has served to confuse the public and others who have to deal with the subject because of legislative or regulatory mandate.

The public basically agrees with the argument that animal research is necessary [according to most polls, about 75 percent accept the practice (1)] but many are not entirely comfortable with the fact that their health is dependent on a practice that often causes death and possible distress of animals. Thus, the public comfortably supports the use of animals in research and medicine when there is a direct benefit for a human and little or no apparent distress caused to an animal. However, when there is apparently much distress and no immediate and obvious benefit to humans, public opposition is relatively easily mobilized.

Discomfort over the need to use animals in research and testing may also be observed among many who work in the laboratory (2,3). When I have specifically asked whether or not a scientist would use an animal if he or she did not need to, nearly all state that they would not. Current legislative mandates and organizational policy statements also imply this premise and urge scientists to use as few animals as possible and then only when necessary.

Some abolitionists believe that all animal research should stop today while others are willing to be more pragmatic. Most animal welfare supporters would like to see the end of animal use in research but do not perceive this to be a realistic or practical goal at the moment. Instead, they believe that the research establishment should devote more time and money to finding ways to eliminate animal pain and distress in research techniques (i.e., the three R's--Reduction, Refinement, and Replacement). While supporting the concept of alternatives in principle, the average scientist still seems to be confused over what should be done to develop and promote these techniques more aggressively, and over how they should meet the new regulatory requirement to search the information base for possible alternatives. Then, there are some scientists who mistakenly see the term "alternatives" as a plot by all animal activists to stop all animal research.

If we are to develop an effective debate on the public policy aspects of animal research and alternatives, we should focus not on the question of whether animals should be used at all (although this is a legitimate issue albeit supported by only a small proportion of the public), but on how we might reduce both animal distress and the number of animals used in the laboratory. The concept of alternatives to animal use and the appropriate level of government effort to develop and promote the concept are key elements in such a debate.

The concept of alternatives is relatively simple and was first enunciated in 1959 by two British scientists who argued that animal researchers should always follow the principle of the "Three R's"--Replacement, Reduction and Refinement (4).

Replacement refers to situations where non-animal techniques may be substituted for techniques using research animals. There are a number of examples of such replacement in the diagnosis of disease and in the testing and standardization of biological therapeutic agents. Rabbits are no longer used in pregnancy tests. Using mice to test the potency of batches of yellow-fever vaccine was long ago replaced by a cell culture test. We may be close to eliminating the use of mice in insulin-standardization procedures as a result of a variety of technical advances.



Reduction refers to cases where the number of animals required for a particular activity or project can be reduced. One example of recent progress comes from the field of acute toxicity testing. Most toxicologists now agree that it is not necessary to use from 60 to 200 rodents to generate the statistically precise lethal dose. One can obtain perfectly adequate lethal-dose data using no more than 10 to 20 animals (5,6).

Another spectacular example of a reduction in animal use comes from the National Cancer Institute's (NCI) drug research and development program. A few years ago, NCI was reportedly using as many as 4.5 million rodents a year to screen chemicals for anti-tumor activity. However, the standard animal model system was far from ideal. After much argument and debate, NCI switched to the use of cell culture screening systems using human cancer cell lines. The program now uses between 500,000 and 1 million mice, an 80- to 90-percent reduction in animal use. It should be noted that the decision to switch was made for scientific rather than animal welfare reasons, illustrating the point that the pursuit of alternatives is not, in and of itself, anti-science.

Refinement is a very neglected aspect of the alternatives concept. It refers to the modification of a technique to reduce the pain and distress experienced by research animals. For example, various jacket and tether systems have been developed to protect catheters inserted into research animals which then allow an investigator to administer doses of test chemicals and take blood samples from an animal without having to restrain it. Capture and restraint often cause significant distress to an animal, so the use of the jacket and tether constitutes a real refinement.

The reduction of pain and/or distress is a popular topic now because Institutional Animal Care and Use Committees (IACUC's) at research institutions are deciding how to respond to the new regulations from the U.S. Department of Agriculture (7) and the guidelines from the National Institutes of Health (8). Principle investigators are now required to minimize animal pain and distress in their research projects (7). In their discussions, the committees should recognize that alternatives are nothing more than new techniques that should help scientists do their job more efficiently and effectively.

Alternatives differ in a significant way from the usual scientific search for new techniques because they require that the use of animals or animal pain and distress be reduced as a result of their implementation. Given the current state of our knowledge, it would be ridiculous to argue that the present rate of advance in the development of biomedical knowledge could be maintained without animal research. But today's refinement may be replaced tomorrow by a new technique that uses no animals. And the development of new research techniques that have also allowed us to reduce the use of laboratory animals in research or the distress caused them has been an important element in the current success of biomedical research. For example, in the development of the polio vaccine, the Nobel prize was awarded to the authors of 1949 cell culture paper. Techniques of human and animal cell culture have been enormously improved since then, and the range of questions that can be investigated and answered in cell culture has expanded commensurately.

A powerful and convincing argument can be made that the development of new research techniques (e.g., paper chromatography, radioimmunoassay, monoclonal antibody production, genetic engineering, polymerase chain reaction, and positron emission tomography, to name a few) has been a critical factor behind rapid advances in biomedical knowledge. Since an alternative is nothing more than a new technique that also happens to lead to reduced animal use and/or distress, I find it hard to see how the pursuit of alternatives could be inimical to science. Toxicologists have begun to embrace the alternatives concept in the last few years, but many other branches of science avoid the issue as much as possible despite considerable public and congressional pressure to do something about "alternatives."

Part of the resistance to the issue of alternatives is the common misunderstanding that the term refers only to replacement. At a talk I gave, I was once introduced as an expert on alternatives. The moderator proceeded to define the term as referring to the three R's and then stated that, although there are a number of alternatives in toxicology, there are none available in cardiovascular or behavioral research. The moderator had fallen into the classic error of defining the term as the three

R's and then thinking only in terms of one R, replacement. There are clearly opportunities to explore reduction and refinement in cardiovascular and behavioral research.

When principle investigators (PI) search for documentation that they have considered but rejected as alternatives, they should consider whether their use of new anesthesia and post-operative husbandry techniques may be identified as an alternative. IACUC's and PI's must incorporate not just replacement but also reduction and refinement into their planning and consideration of animal research protocols.

It is obvious to anyone who is able to step back from the laboratory bench and review the public's attitudes toward science that there is concern, not just about animal abuse, but also about any use of animals. In the 1960's, a scientist could feel like a public hero. Today, he or she may be made to feel like a criminal. In the last 10 years, the membership of animal protection groups has increased fivefold to tenfold. Symbols of public concern for animals are widespread throughout popular culture. Even Superman has been drawn into the animal research controversy. In a recent issue of the comic book, Lois Lane exposed a callous biomedical researcher, and Superman had to subdue the monstrous ape resulting from the research, if possible, without killing it!

The public wants alternatives developed and promoted. Scientists can satisfy these public concerns without compromising the quality of their research. To continue the polarized argument about whether or not animals are needed in research is unproductive. Scientists can show the public that they are greatly concerned about research animal use and distress by instituting and publicizing programs that actively seek ways to reduce animal use and distress, and increase the well-being of laboratory animals.

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# Effects of the Shift to Alternatives on Industrial Practices

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## Introduction

The intent of this article is to provide an overview of industrial proactivity in embracing the 3R's of alternatives--refinement, reduction, and replacement. Because of the diversity of industrial product lines, one can appreciate that one shoe does not fit all in terms of regulations, politics, marketing, and public opinion. It would be inappropriate to describe industry as a single entity in addressing alternative activity, but it does lend itself to analysis along the four classical industrial groups: cosmetics, household and industrial chemicals, pharmaceuticals, and medical devices.

In reality, public opinion has already broken industry up into categories if one acknowledges public sentiment regarding animal testing. Two 1990 polls, a Gallup Poll printed in *Advertising Age* and an unpublished Roper Poll conducted on behalf of industry, denoted similar data referencing society's impression of the use of animals in product testing (9, 6). These polls found that only one-third of those surveyed condoned use of animals in the testing of cosmetics and household products. About one-half of those polled accepted animal usage in research for over-the-counter drugs, whereas the use of animals in testing of prescription drugs and medical devices was accepted by about two-thirds to three-quarters of those surveyed. One may venture the generalized statement that whereas drugs and medical devices appear to be viewed by the general public as necessities, cosmetics and household products appear to be viewed by the same public as niceties.

## The Cosmetics Industry

The cosmetics industry is a \$45 billion a year business with thousands of products embodied in 33 Food and Drug Administration (FDA) classifications (13,18). Cosmetics are defined by the Food, Drug and Cosmetic Act as "articles intended to be applied to the human body for cleaning, beautifying, promoting attractiveness or altering the appearance without affecting the body's structural function" (8). The key words in this definition are "intended" and "body's structural function." Intended use of the cosmetic must be clearly labeled and if the safety of a cosmetic product is not adequately substantiated for that intended use, the product is considered misbranded and may be subject to regulatory action. The physiological, or functional, altering of the body differentiates drugs from cosmetics. The FDA regulates this difference by not requiring premarket approval of cosmetics. At the same time, however, the FDA does expect that the manufacturer of a cosmetic has conducted toxicological and other appropriate tests to substantiate the safety of the product and can provide these data if challenged by the agency. While it has become fashionable for some manufacturers to apply the "cruelty-free" label to their products (indicating that animals were not used during safety testing), this claim can be misleading (see sidebar--The Cruelty-Free Label).

In vitro tests and other nonanimal methods for safety evaluation have come a long way and are being used in industry as initial screening procedures. However, given a new cosmetic derivative or a cosmetic incorporating a drug component, a standardized in vivo test, such as the Draize Ocular Irritation Test, may be in order. This in vivo test is still considered valuable in predicting human eye irritants when the irritation is subtle or when the chronic recovery phase data may be equally as important as the initial acute exposure data. Industry, in cooperation with regulatory agencies, has established multiple refinements to obtain the required data while minimizing the potential for pain or distress. Evaluation of the agent's pH and primary dermal irritation tests are routinely used to screen out agents likely to evoke a response beyond moderate irritation (17). Agents having passed

the preliminary screening could conceivably go on to the classic test but with the following refinements in place: use of three animals vs. the standard of six; use of smaller volumes of solution installed in the eye; use of one animal to evaluate an unknown and await a response before continuing or discontinuing with the remaining test animals; and use, when applicable, of anesthetics in the eye (10). In part, because of refinements to the Draize Ocular Irritation Test and use of available in vitro methods, the number of rabbits used in the cosmetics industry between 1980 and 1989 was reduced by 87 percent (12).

## **Chemical and Household Products Industry**

The household and industrial chemical group is extremely diverse, touching all our lives every day in the home, the workplace, and the outdoors. The Environmental Protection Agency (EPA) has listed over 100,000 chemicals in our environment, with several thousand new chemicals being added each year (11). The definition of this group is "those products that are of a non-medical nature that are created to enhance personal, household, industrial and agricultural applications." This group is also under attack by animal activists and, in fact, PETA has a top 50 product boycott list that includes many companies supplying these products (4). However, the chemical and household products group, unlike the cosmetics group, is frequently called on by government agencies to provide safety data obtained from in vivo testing. A risk assessment of a given chemical may be required by the Department of Transportation (DOT) to classify chemicals for handling and transportation, the Occupational Safety and Health Administration seeking to protect workers via the manufacturer identifying "gross, mostly local toxic effects," and the Environmental Protection Agency to assess the potential environmental impact of a product's release into the environment. Needless to say, the general population expects the manufacturer to provide toxicological data should there be accidental or deliberate exposure. The poison control centers in the United States receive on average 1.6 million calls a year; 900,000 of these calls relate to accidental poisoning of children and about 40,000 to animal poisoning. (14) The bottom line is an obvious need to safeguard the general public from accidental injury and to acquire the essential information through effective product testing.

In the area of alternatives for this industrial group, we find the introduction of the Corrositex Test. This test, introduced in 1993, marked the first acceptance by a Federal agency (DOT) of an in vitro test as an alternative to animal testing for regulatory purposes (21). The corrosive classification of a given chemical can be determined by this test based on the time it takes the chemical to cause damage to a collagen matrix top layer, which approximates a full-thickness layer of skin cells, and elicit a color indicator response in a second layer. Although there are categories of chemicals for which this test is not applicable, it has been shown to be 97.7 percent accurate in identifying all commercially available corrosive chemicals on the DOT Hazardous Material Table (5).

## **Pharmaceutical Industry**

A drug is defined as "an article intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in humans and other animals; and articles (other than food) intended to affect the structure or any function of the body of humans or other animals." (8) The pharmaceutical industry is an area of great potential for development of alternatives to animal testing. Whereas cosmetic/consumer products impart their benefit with little or no effect on physiological functions, drugs purposely affect the biological processes controlling life. As a consequence, drug interaction necessitates considerable investigation to ensure both efficacy and safety. Drug introduction to market is an extremely expensive and time consuming endeavor. While a cosmetic may take but 6 months to reach the consumer, and a typical consumer/industrial chemical 2 to 3 years and \$1 to \$2 million to get to market, that is but a blink of an eye and pocket change to the drug industry (18). In the process of drug development and approval, an average of 6.5 years is spent in the screening and preclinical testing of as many as 5,000 candidate compounds. Only 5 of 5,000 compounds that enter preclinical testing make it to human testing, which consumes another 6 years. FDA review and approval entails on average another 2.5 years, and typically only 1 of the 5 drugs will be approved. The bottom line is an average of 15 years from laboratory to medicine chest at an investment cost of



\$359 million. The Pharmaceutical Research and Manufacturers of America estimates that this will reach \$1 billion in cost per drug early in the next century (2).

Although the cost and time associated with clinical testing and FDA review may be inescapable now and in the future, use of in vitro methods in the discovery and preclinical phase has been instrumental in streamlining these stages. Computer modeling and structure-activity relationships have been invaluable in the early screening of candidate drugs. Agar overlay for cytotoxicity, Ames mutagenicity assay, cell transformation assay, and yeast mutagenicity assay are among those tests in common use for early toxicity screening. In the preclinical phase, a meaningful reduction in animal numbers has been attributed to use of tiered testing, approximate lethal dose, and the Up and Down Method to replace the classic LD50 (3).

## **Medical Device Industry**

Finally, there is the medical device industry. Medical devices are defined as, "any health care product that does not achieve any of its principal intended purposes by chemical action in or on the body or by being metabolized" (8). This group consistently fares well in animal use surveys likely because of the perception by the general public that the products they produce have immediate and measurable impact on the quality of life and the saving of lives.

To accomplish their intended purpose, medical devices require varying degrees of invasiveness, which in turn necessitates various levels of safety and efficacy testing. Medical devices are evaluated by a scheme consisting of a battery of in vitro and in vivo tests (19). For those devices that are in contact with the intact skin only, the normal scheme requires the:

- 1) intracutaneous irritation test in the rabbit
- 2) maximization test for hypersensitivity in the guinea pig
- 3) cytotoxicity via agar overlay
- 4) acute systemic test in mice

For those medical devices passed into the body, such as catheters, the testing includes 1-4 above plus:

- 5) in vitro hemolysis in whole blood
- 6) rabbit pyrogen or in vitro Limulus amoebocyte lysate (LAL) for pyrogenic effect
- 7) rabbit muscle implants for biocompatibility
- 8) Ames mutagenicity to evaluate mutagenic potential

For those devices implanted for a period in excess of 30 days, such as heart valves, tests 1-8 are required as well as:

- 9) chronic toxicity
- 10) carcinogenesis testing

In reviewing the tests making up the evaluation scheme, a major area for development of alternatives is that of biocompatibility testing. The interaction of implanted biomaterials on the body tissues is an area that has received much attention as a result of the controversy surrounding breast implants. The present in vivo methods involve a considerable investment of time and resources with enough scientific uncertainty in the results to suggest the need for the investigation of in vitro methods to either replace or supplement these tests. In the meantime, the medical device industry has done a good job of embracing alternative methods for training. Such implements as surgery computer simulation, foam cadavers, mannequins, use of cadaver tissues for laser training, and the laparoscopic "black box" have been useful adjuncts in common use in this industrial group. In the research and development phase, such refinements as telemetry implants, vascular access ports, and electronic access ports have been well received alternatives to more invasive data collection methods.

## **Industrial Survey**

To augment this general overview of how alternatives affect industrial practices, a small (n=14) informal survey was conducted among companies representing the cosmetics/chemical and drug/medical device industries. The intent of the survey was to ascertain the general attitude of the

industries towards the consideration, or experience in use, of alternative methods. In general, all industries indicated an appreciation for the coming of age of alternative methods; however, as one might predict there was a difference of opinion between the two groups. Questions were presented with a range response of "strongly agree" to "strongly disagree" with additional comments encouraged. Those questions invoking the most interesting responses are noted below:

1. "Your firms' move to consideration of alternatives is/was influenced by the animal activism movement"? The response was not too unexpected as cosmetics/chemical companies indicated an agreement to strong agreement with this statement. Drug and medical device companies were neutral to indicating disagreement with the statement. This result aligned well with the public opinion of increased acceptance of animal usage for the drug and medical device industry.
2. "Your firms' move to consideration of alternatives is/was influenced by direct monetary considerations"? The response for the cosmetics/chemical group was somewhat surprising. One would expect that some test cost savings would be achieved by these groups given their significant experience with nonanimal alternatives. However, the majority responded as disagreeing with the statement. The plausible explanation is that even if cost savings are presently being realized, use of alternative tests has yet to recover the costs of development and validation of these methods. Drug and medical device companies were neutral on this question, likely indicating inadequate experience to pass judgment.
3. "Your firms' move to consideration of alternatives is/was influenced by indirect monetary considerations"? Both cosmetics/chemical and drug/medical device companies were neutral when answering this question on using alternatives as a marketing tool. Given the use of "cruelty free" advertising by some beauty product firms, this result may seem inconsistent on the part of the cosmetics firms. However, the cosmetics companies surveyed were major reputable companies claiming a strong aversion to seeking a market advantage through such advertising.

Each group was surveyed as to their main change in business practices since the advent of alternatives. The cosmetics/chemical group emphasized public opinion aspects, notably: Animal work is reviewed at a much higher administrative level, use of human subjects is increased, and much stronger public relations departments are established. The drug and medical device group laid most emphasis on scientific enhancements, noting increased management involvement in test selection, an enhanced level of innovative thinking about the feasibility of alternatives, and a noticeable improvement in acceptance and use of validated nonanimal methods.

When questioned on what nonanimal tests were being used by their firms, the groups reported that: All are currently using structure-activity relationships, deductions based on similar products, cell cultures, and comprehensive literature searches for toxicity of raw materials. The cosmetics and chemical industries use commercially available artificial tissues and drugs/medical device industries use well-established in vitro methods such as agar overlay for cytotoxicity, Ames mutagenicity assay, and cell transformation assay. Given the opportunity to add to this survey list, the cosmetics/chemical group noted that they are using the bovine corneal opacity test, chorioallantoic membrane test, and yeast phototoxicity assay. Drug and medical device groups are using combinatorial chemistry, gene sequencing, and tissue slices.

## **The Worldwide Picture**

The industrial market is a worldwide market, so legislation affecting one region can have significant repercussions on the far side of the globe. Such may be the case with impending enforcement of legislation in Europe. In 1986, Directive 86/609/EEC was passed into law establishing a European commitment to the 3R's--reduction in number of animals used, refined techniques to minimize pain, and replacement of live animals with nonanimal techniques. In particular, article 7.2 states, "An experiment shall not be performed, if another scientifically satisfactory method of obtaining the result sought, not entailing the use of an animal, is reasonable and practicably available." In 1991 the Commission of the European Communities consummated the push for alternative procedures by establishment of the European Centre for the Validation of



Alternative Methods (ECVAM) (20). This melting pot of European scientists was tasked with coordinating the validation of alternative test methods, functioning as a focal point for information exchange, establishing and managing an alternative database, and promoting an international dialog for encouraging development, validation, and regulatory acceptance of alternative test methods (1). This sequence of events took on potential worldwide market impact when on June 14, 1993, the Council of Ministers approved a 6th Amendment to the Cosmetic Directive 76/768/EEC. The preamble of this document includes the following background statement with reference to cosmetics: "whereas testing on animals of ingredients or combinations of ingredients should be banned as from 1 January, 1998."

The directive came with the loophole that should the ECVAM scientists not demonstrate scientifically equivalent nonanimal test methods, the deadline could be extended minimally another 2 years (15). However, ECVAM progress to date would indicate the probability of some methods meeting this criterion by the January 1, 1998 date (16). [Ed. note--At a Scientists Center for Animal Welfare symposium on toxicology, held in Baltimore, Maryland on June 9-10, 1996, Dr. Alan Goldberg, Director, Johns Hopkins Center for Alternatives to Animal Testing, stated that it now appears that the EC directive will initially apply to testing on final products and not individual ingredients. A decision on the fate of testing on individual ingredients will come later.]

The potential impact of the EEC Directives is of future concern mostly from the perspective of interpretation. The question may be asked, "Will U.S. regulators accept European alternative methods and validation procedures? Will there be an agreement on the vagueness of ingredients vs. final formulation?; that is, if a U.S. company initially develops a product with intent for it to be a drug, thereby likely requiring some animal testing, what if later it is not efficacious as a drug but would suit as a cosmetic. Does the initial animal testing of the chemical disqualify it for later reclassification? Will the varying U.S. and European definition of cosmetics result in major consequences for multinationals (that is, trade barriers)? For example, in the United States, such products as sunscreens, antiperspirants, antibacterial soaps, and fluoride tooth paste are considered drugs, whereas in Europe they are considered cosmetics. A company is, thus, in the potential bind of satisfying U.S. regulators by performing safety animal testing only to be disqualified in the European market with the same product because it has undergone animal testing.

## Conclusions

It is perhaps fair to say that at this point in time the cosmetics and, to a lesser degree, the chemical industries have embraced alternative methods that primarily support the R's of reduction and replacement. The drug and medical device industries have likewise demonstrated success in the R of reduction and meaningful advancements in refinements. The R of replacement is likely a long-term consideration for the drug and device industries given the complexity of their respective chemical/material entities and their purposeful direct interaction with the body. It is generally encouraging to see the extent of alternative usage or at least consideration of alternatives across all of the industrial groups surveyed. It is apparent that, for the future, the financial impact of market barriers resulting from laws requiring alternatives may be a far greater direct influence on development and use of alternatives than public opinion and the animal activism movement. As in vitro tests are developed and validated, and harmony is established between regulatory bodies and international groups, the full spectrum of the 3R's will be hopefully realized.

For more information, Dr. Walker may be contacted at phone: (612) 736-3747, fax: (612) 736-1519, e-mail: [dhwalker@mmm.com](mailto:dhwalker@mmm.com) or by writing to 3M Corporation, Bldg. 270-2A-08, 3M Center, St. Paul, MN 55144-1000.

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# AWIC Tips for Searching for Alternatives to Animal Research and Testing

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This article is available at <http://www.nal.usda.gov/awic/alternatives/tips.htm>

*Editor's note: Mention or use of a trademark does not constitute endorsement by the United States Department of Agriculture.*

The following guidelines were developed to assist researchers, information specialists, and Institutional Animal Care and Use Committee (IACUC) members, when conducting literature searches to determine if alternatives to the use of animals exist and whether a protocol unnecessary duplicates previous research. When searching for alternatives, the staff at the Animal Welfare Information Center (AWIC) refer to the tenets of the 3 R's introduced by W.M.S. Russell and R.L. Burch(1959) in their book *The Principles of Humane Experimental Technique*<sup>1</sup>. The 3 R's represent reduction in the number of animals used, refinement of techniques and procedures that reduce pain and distress, and replacement of animal with non-animal techniques.

The first step in conducting a search for alternatives, involves communication between the investigator and the information specialist. The specialist cannot effectively search for alternatives without a basic understanding of the type of research the investigator is proposing. The most efficient means of communicating is a direct dialogue between the investigator and the information specialist. A third party should not be used to convey information.

Investigators can assist information specialists by being prepared to give precise and specific information about their research or testing procedures. The following may serve as a guideline for the type of information the investigator may be asked to provide:

- 1) What is your general area of study (e.g., cardiology, neurology, toxicology, etc.)?
- 2) What species are you currently working with (e.g., rats, dogs, swine, etc.)?
- 3) Briefly describe your experimental protocol.
- 4) What specific systems or parts of the anatomy are involved (e.g., central nervous system, brain stem, parabrachial nucleus)?
- 5) Please give correct spellings of these structures and any acronyms (e.g., CNS, PBN). European and British spellings are important as well.
- 6) If you are studying the effects of a particular hormone, enzyme, or chemical agent, please give the complete spelling of the compound as well as its trade name and acronym (e.g., bovine somatotropin, BST).
- 7) Do you know of any prominent authors in your area of research? Have you published any previous literature that relates to your current study?
- 8) What makes your study unique from previous studies (e.g., testing a new technique, investigating a new compound, further understanding of a biochemical pathway)?
- 9) Are you aware of any possible alternatives to your research, such as experiments conducted on alternative species, cell culture, or in vitro studies?
- 10) Have you had any other searches conducted for you? If so, what databases were used (e.g., MEDLINE, AGRICOLA, BIOSIS)?
  - a) What keywords were used (e.g., kidney, parathyroid hormone)?
  - b) What years were searched (e.g., 1985-present)?

As with any type of searching, success in retrieving relevant citations will depend directly on the quality of the information provided.

## **Search Strategy**

Once the initial exchange of information has taken place, the information specialist can begin to formulate a search strategy. Search strategies for alternatives may be divided into two phases, reduction and refinement, and replacement.

### **Phase I (Reduction and Refinement)**

Phase I consists of a generalized database search used to retrieve citations pertinent to the investigator's field of study. Citations retrieved during this phase, should provide information on current research, alert the investigator to whether or not they are performing duplicative studies, and possibly provide information to refine experimental techniques.

During Phase I, the information specialist may find it helpful to develop search strategies using databases available on Compact Disc Read Only Memory (CD-ROM). AGRICOLA, MEDLINE, TOXLINE, and LIFE SCIENCES, are examples of several useful databases available on CD-ROM. Searching on CD-ROM allows the information specialist the freedom to experiment with keywords, explore indexes and thesauruses, and read abstracts without the pressure of being charged for online time. If the investigator has published previous literature this is a good time to read abstracts of his or hers previous work and become familiar with terminology used to describe the study and to note what terms were used to index the abstract. Searching on CD-ROM should provide the information specialist with a general idea of how much literature exists on a specific topic. If few relevant citations are found, the information specialist may need to broaden the search strategy or use the expanded capabilities of online database searching to develop the search. If hundreds of citations are retrieved using only a few years worth of bibliographic data, then it is necessary to further consult with the investigator on ways to narrow the search.

### **Phase II (Replacement)**

Upon completion of Phase I, the information specialist should have a basic understanding of the research area including: 1) the literature published in the particular field, 2) the techniques used, and 3) the commonly used species. The information specialist is now ready to search for possible replacement alternatives.

The following questions may be used to assist in the search for replacement alternatives:

- 1) Are there in vitro techniques that may reduce or replace the number of animals used (e.g., chorioallantoic membrane assay, use of primary cultured hepatocytes)?
- 2) Are there any alternative animal models (e.g., invertebrates, fish, protozoa, etc.)?
- 3) Have any computer simulations or statistical models been developed that relate to the study?

When searching for alternatives, information specialists should search multiple databases. A multidisciplinary approach to searching may yield surprising results particularly for individuals who are not accustomed to searching the literature outside their general area of study, (e.g., Medicine). AWIC provides a factsheet entitled Databases for Biomedical, Veterinary and Animal Science Resources 2 that describes a number of useful databases.

"Animal testing alternatives" is a phrase used to index citations regarding alternatives in the AGRICOLA, MEDLINE, TOXLINE, and CANCERLIT databases. However it is not used to index alternative studies in other databases such as EMBASE, BIOSIS PREVIEWS, LIFE SCIENCES, and CAB Abstracts. Although useful, this phrase should never be the only strategy used to retrieve information on alternatives. Depending on the study, other terms such as tissue culture, cell culture, in vitro, simulation, model, refinement, reduction, or alternative may be used. For a listing of terms

that may be helpful when conducting alternative searches information specialists may refer to Animal Welfare Information Center Scope Notes<sup>3</sup> available from AWIC at no charge.

It is important to keep in mind that although electronic databases are powerful resource tools, most databases do not index journals before the mid-sixties and relevant information from early studies will not be retrieved. In addition, information on alternatives is available in newsletters, books, and proceedings, which not all databases index.

**Sample Search for Alternatives**

The following is an actual search that was requested by an IACUC member and a description of the steps that the AWIC information specialist performed. The IACUC member requested a search for alternatives to the use of zona free hamster oocytes to test human sperm penetration, motility, and viability.

After initial information was exchanged about the protocol, a list of keywords were developed. The specialist then conducted a brief initial search on MEDLINE and AGRICOLA on CD-ROM to become familiar with abstracts in which human sperm penetration, motility, and viability were tested. The specialist was aware that extensive tests have been developed to assess semen characteristics in domestic farm species and therefore contacted a farm animal reproductive physiologist for further information. The physiologist confirmed that alternative methods exist to test bovine and human sperm penetration such as a variety of cervical mucus tests. Based on this information the specialist developed the following search strategy.

**Databases Selected**

Thirty five different biological and medical databases were selected and searched simultaneously including BIOSIS PREVIEWS, AGRICOLA, CAB ABSTRACTS, CRIS, PASCAL, MEDLINE, EMBASE, PHARMACEUTICAL HEALTH CARE INDUSTRY NEWS, LIFE SCIENCES, SCISEARCH and others.

**Search Strategy**

Set	Items*	Description
1	214550	SPERM OR SPERMATID? OR SPERMATOZOA? OR SEMEN
2	1104759	MOTILITY OR VIABILITY OR MORPHOLOGY OR MOTILE OR VIABLE
3	45369	S1 AND S2
4	42329	S3 NOT HAMSTER
5	1384	S4 AND (MUCUS OR MUCOUS)
6	1049	S5 AND HUMAN
7	364	S6 AND PY=1988:1993
8	191	RD S7 (UNIQUE ITEMS)
9	154	S8 AND (EVALUAT? OR ANALYSIS OR TEST? OR VITRO)
10	94	S9 AND PY=1990:1993
11	2	S4 AND (COMPUTER(2N)IMAGING)

\* ITEMS = number of citations retrieved that contain search terms



## **Sample Titles Retrieved**

Hyaluronic acid as a medium for human sperm migration tests.

Keywords: cervical mucus, spermatozoa, penetration.

Human sperm-cervical mucus interaction using bovine cervical mucus and hen's egg white in the evaluation of male infertility.

Keywords: penetration, sperm motility, physiological model, in-vitro test.

The use of hen's egg white as a substitute for human cervical mucus in assessing human infertility.

Keywords: penetration, semen analysis, sperm capacity, sperm motility.

Comparison of measurements of human sperm motility characteristics by the automated CELLSOFT system and time exposure photomicrography.

Keywords: automated analysis, sperm motility.

In this case, consultation with an expert and review of the literature supported information available on replacement alternatives. If that had not been the case the search may have focused more on refinement and/or replacement alternatives. The IACUC may have asked, what methods are being used to superovulate and flush oocytes from the hamster, how are the hamsters anesthetized during procedures, and what are the fewest number of animals that can be used?

## **General Comments**

Protocols should be evaluated on a case by case basis. A perfect strategy to retrieve every citation regarding reduction, refinement, and replacement does not exist. Many factors may affect the outcome of a literature search, including the area of research, species involved, procedures used, chemical(s) tested, experimental design, and whether or not articles have been indexed. Additional factors include: 1) the degree of communication between the information specialist and the investigator, 2) the knowledge and educational background of the information specialist, and 3) time and money constraints.

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Bielenberg, K. and D. Berry. (December 1990) *Databases for Biomedical, Veterinary and Animal Science Resources AWIC Fact Sheet*.

Swanson, J. (March 1991) *Animal Welfare Information Center Scope Notes. AWIC Series #6. 8 p.*

## **Additional Resources**

Clingerman, K., C. Dowling, and J. Swanson. (June 1990) *Searching AGRICOLA for Animal Welfare STS-03. June 1990. 20 p.*

Kreger, M. and T. Allen. (October 1993) *Electronic Information for Animal Care and Use. Lab Animal 22(10):52-53.*

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# On-line Databases

## What is Available? What is Missing?

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*Editor's note: This paper is adapted from a talk given at the Second World Congress on Alternatives and Animal Use in the Life Sciences held in Utrecht, The Netherlands in 1996.*

*[Mention of commercial enterprises or brand names in the following article does not constitute endorsement or imply preference by the U.S. Department of Agriculture. The views expressed by the author do not necessarily represent positions or policies of the U.S. Department of Agriculture or any agency thereof and should not be interpreted as such.]*

It has been the Animal Welfare Information Center (AWIC) staff's experience that many researchers looking for alternatives to painful procedures or the use of animals search only Medline and ignore other databases that index biomedical, biological, and bioengineering literature, computer hardware and software, or audiovisuals. However, as will be seen, there are many comprehensive and specialty databases that should be examined. This discussion will review a number of commercially available databases highlighting the strength and weaknesses of each as they pertain to the use of animals or alternatives in research. It will also briefly look at a multi-database searching technique and terminology used by AWIC staff to find alternatives.

While these sources will provide the user with a wealth of information, they can not provide information that is not made available by the scientific community. The publication of negative scientific results and/or specific conditions affecting animals used in experiments, use of alternatives terminology when abstracting journal articles or assigning keywords, and standardization of indexing terms for alternatives are several areas that would greatly benefit the search for alternatives.

### COMMERCIAL/GOVERNMENT DATABASES (in alphabetical order)

Information in this section was obtained from DIALOG Blue Sheets, WWW, and experience using the database. DIALOG Blue Sheets, which contain descriptive information about the databases found on DIALOG, can be found at <http://library.dialog.com/bluesheets>

DIALOG is an information service that provides access to more than 450 databases covering a range of disciplines. Subscription information can be obtained from Knight-Ridder Information, Inc., 2440 El Camino Real, Mountain View, California 94040, USA; tel: (415) 858-3785; WWW: <http://www.dialog.com/>

### AGRICOLA (AGRICulture OnLine Access)

AGRICOLA is produced by the U.S. Department of Agriculture's National Agricultural Library (NAL) and covers the period from 1970 to the present. One of the major strengths of this database is its inclusion of a variety of information sources. The materials covered in this database consist of articles, notes, letters, or chapters from peer-reviewed journals, popular magazines, newsletters, books, theses, patents, translations, audiovisuals, software, technical reports, and Congressional documents related to agricultural and animal welfare issues. Subject coverage includes agriculture in its broadest sense, alternatives to animal testing, animal behavior, animal sciences, animal welfare, laboratory animal medicine, physiology, veterinary medicine, wildlife, and zoology. It is especially strong in veterinary anesthesiology for farm animals, dogs, cats, and increasingly so for laboratory animals. The *CAB Thesaurus* is the basis for controlled vocabulary indexing. Both AGRICOLA and CAB ABSTRACTS index using the phrase "animal testing

alternatives." A search performed in AGRICOLA in October 1996 using this phrase retrieved 693 records. However, one of the complaint is lack of information concerning drugs, chemicals, enzymes, etc. used in a study. It would be useful to have Chemical Abstract Service (CAS) registry numbers added in a descriptor field or, at the very least, list all pertinent compounds used in a study.

At the present time, AGRICOLA indexes more than 1,400 journals including many types of grey literature (pamphlets, conference reports, etc.) that are difficult to locate. AGRICOLA is available from DIALOG as File 10. AGRICOLA can also be searched on the WWW at <http://www.nal.usda.gov/ag98/ag98.html> Information about AGRICOLA can be found at [http://www.nal.usda.gov/general\\_info/agricola/agricola.html](http://www.nal.usda.gov/general_info/agricola/agricola.html)

## BIOSIS Previews

BIOSIS Previews is a comprehensive biological and biomedical database containing more than 12 million citations. As with AGRICOLA, this database also includes a variety of information types such as journals, meeting abstracts, reviews, books, notes, letters, institutional and government reports, and research communications. Subject coverage includes all the life sciences such as agriculture, behavior, biotechnology, cell biology, pharmacology, physiology, radiation biology, toxicology, veterinary science, etc. According to BIOSIS, there is no thesaurus or controlled vocabulary used (personal communication, 1996). Several years ago, BIOSIS considered either developing a separate database on alternatives or devising a new indexing system to make searching for alternatives more practical. It was finally decided that there was not enough interest in the topic within their user community to warrant a separate database and that the indexing system in place was adequate to address searching for alternatives. In spite of those decisions, BIOSIS remains a tremendous resource for those looking to implement alternatives into their studies. A problem with searching BIOSIS on DIALOG as part of a multidatabase search is that duplicate detection is not supported. Because of the style in which BIOSIS is configured, duplicate records are not detected by the DIALOG system when the *remove duplicates* command is given.

At the present time, BIOSIS indexes almost 10,000 journals and monographs each year. It is available as File 5 (1969-present) or File 55 (1985-present) on DIALOG. The BIOSIS website can be found at <http://www.biosis.org>

## CAB ABSTRACTS

CAB ABSTRACTS is probably the world's most comprehensive database for agriculture, animal health, veterinary medicine, and increasingly, laboratory animal medicine, husbandry, and welfare. This database indexes more than 11,000 journals, as well as books, serial monographs, reports, newsletters, theses, symposia and conference proceedings, bibliographies, and translations. Most of the records contain abstracts. The *CAB Thesaurus* is the basis for controlled vocabulary indexing. It should be noted that AGRICOLA does not usually index materials that can be found in CAB ABSTRACTS. Subject coverage includes agriculture in its broadest sense, animal health, animal production, animal sciences, animal testing alternatives, animal welfare, laboratory animal medicine and husbandry, veterinary medicine and science, and related topics. Unlike AGRICOLA, CAB provides very specific information with each record. CAS registry numbers makes it very simple to locate records pertaining to specific chemical compounds and organism descriptors makes it easy to search for information by species, breed, variety, etc. Although *animal testing alternatives* is used as an indexing term, a quick search of the database done in October 1996 using this phrase retrieved only 30 records. The reason for the lack of records will be discussed later.

At the present time, CAB ABSTRACTS contains more than 3 million records. It is available on DIALOG as File 50 (1972-present) and is also available as a CD-ROM. The CAB Abstracts Database website can be found at <http://www.cabi.org/infolib/cababdb/cababdb.htm>



## EMBASE

EMBASE is produced by Elsevier Science Publishers in the Netherlands and covers the period from 1974 to the present. It is an important database to use when looking for alternatives to animal research because it indexes articles and notes from journals, conferences, symposia, and meetings. Subject coverage includes all aspects of human medicine and in vivo and in vitro biomedical research on topics including but not limited to anesthesiology, cancer, cardiovascular disorders, drug abuse, neurology, ophthalmology, pharmacology, physiology, psychiatry, surgery, toxicology, etc. In general, there is about a 10 percent to 30 percent overlap with Medline on materials indexed, depending upon the subject area. EMBASE also provides extensive documentation of drugs and/or chemicals used in experiments. The July 1995 issue of *Profile: the Excerpta Medicine Newsletter* had an article on searching EMBASE for alternatives to animal testing (anon., 1995). The article advises using their Emtree term "animal welfare" along with terms such as "animal experiment" or "animal model" or "animal testing alternative." However, using the term "animal welfare" only retrieves about 250 records from the entire database. However, the AWIC staff has found EMBASE to be a major source of information on alternatives and always includes this database in any literature search.

EMBASE currently indexes more than 3500 journals from over 110 countries and adds almost 400,000 new records annually to the 7 million records already indexed. It is available from DIALOG as File 72 (1974-present) or File 73 (1985-present). The Elsevier Science website search utility can be found at <http://www.elsevier.com:80/homepage/search.htm>

The website offers free searching of the tables of contents of all journals indexed by Elsevier.

## MEDLINE

MEDLINE is produced by the U. S. National Library of Medicine and covers the period from 1966 to the present. Medline is an exceptional database in that it provides comprehensive coverage of human medicine, animal-based and in vitro biomedical research, and veterinary medicine and science for both farm and laboratory animals. Unlike the databases already discussed, MEDLINE only includes information from peer reviewed journals. Indexing uses a controlled vocabulary known as MeSH (Medical Subject Headings). The database also provides extensive information on drugs and chemicals used in experiments. This information can be found using trade names, chemical names, or CAS registry numbers. MEDLINE indexes articles using the phrases "animal testing alternatives" and "animal welfare." Unfortunately, a search performed in October 1996 found that "animal testing alternatives" retrieves only 404 records, while "animal welfare" finds only 2,006. However, it is an easy database to search using free text terms.

MEDLINE currently contains about 9 million records. It is available from DIALOG as File 154 (1985-present) or File 155 (1966-present). MEDLINE can also be searched using Internet Grateful Med at <http://igm.nlm.nih.gov:80/>

## PASCAL

PASCAL is produced by the French National Research Council's Institut de l'Information Scientifique et Technique and covers the period from 1973 to the present. This is a major multidisciplinary database that provides coverage of chemistry, biology, medicine, biomedical research, neurosciences, biotechnology, zoology (especially invertebrates), and the agricultural sciences. However, it does not cover animal husbandry or veterinary pathology. PASCAL also indexes materials from a variety of sources including journals, theses, conference proceedings, reports, books, and patents. Indexing is accomplished using a controlled vocabulary of more than 80,000 terms. However, free text searching is very easy to perform.



At the present time, PASCAL indexes more than 8,500 journals. This accounts for 93 percent of the database of 11 million records; 7 percent comes from grey literature. According to the PASCAL website, 65 percent of the literature indexed covers the medical and biological sciences. It is available from DIALOG as File 144 (1973-present). The English version WWW address is <http://www.inist.fr/anglais/bbdang/pascal/pascal.htm>

The homepage of the French National Research Council's Institut de l'Information Scientifique et Technique can be found at <http://www.inist.fr/>

## TOXLINE

TOXLINE is produced by the U.S. National Library of Medicine and covers the period from pre-1950 to the present. The types of publications indexed are journals, books, reports, theses, letters, meetings, project summaries, and unpublished materials. Subject coverage includes adverse drug reactions, carcinogenesis, drug evaluation, mutagenesis, pollution, pesticides, herbicides, radiation, teratogenesis, and all other aspects of toxicology. TOXLINE uses the MESH terms discussed in MEDLINE as its controlled vocabulary but again it is an easy database to search free text. Useful terms include "animal welfare" and "animal testing alternatives" although these terms alone are not sufficient to ensure a thorough search for alternative methods. Information on drugs or chemical compounds is easy to find using CAS registry numbers, chemical names, or tradenames.

At the present time, TOXLINE contains more than 2 million records. It is available from DIALOG as File 156. It can also be searched via Internet Grateful Med at the address given above.

A comprehensive listing of databases, including some not mentioned in this discussion, is in Table 1.

Table 1. Databases for Searching for Alternatives

<b>Available on Dialog:</b>	● ASFA - file 44	● NTIS - file 6
● AGRICOLA - file 10	● PSYCHINFO - file 11	● INSPEC - file 2
● MEDLINE - file 154	● SCISEARCH - file 34	● COMPENDEX PLUS - file 8
● EMBASE - file 72	● TOXLINE - file 156	● MICROCOMPUTER INDEX - file 233
● BIOSIS - file 55	● CAB - file 50	● A-V ONLINE - file 46
● LIFESCIENCES - file 76	● AGRIS - file 203	● PASCAL - file 144
● ZOOLOGICAL RECORD - file 185	● INT'L PHARM. ABSTRACTS - file 74	

## MULTI-DATABASE SEARCHING and USEFUL TERMINOLOGY

Several papers have discussed, in detail, strategies for retrieving information on alternatives from databases (Shevell and James, 1995; Smith, 1994; Snow, 1990). Those interested in an in-depth look at developing search strategies are encouraged to read these articles. The first step in conducting a search is to have a clear understanding of the objectives and methods of the proposed study. Too often investigators ask for alternatives to very specific procedures without putting the procedure in the context of an experiment. To properly look for alternatives you have to know why the procedure is being performed and what the expected outcome is.

Once all pertinent information is at hand the literature search strategy can be developed. It is convenient to conduct a search using the 3Rs as a guide. The first part of the search will examine the literature closely related to the proposed study for refinements to the proposed methods, methods or models that will reduce the number of animals used, and to see if the proposed work duplicates

previously published experiments (this is a requirement of the U.S. Animal Welfare Act). The terminology used in this part of the search will come from the area of study. Depending upon the type of research, it might also be important to look for appropriate anesthetics, analgesics, methods of restraint, etc. Also remember to include both American and European spelling of words--for example, anesthesia, anaesthesia, anasthesia. It is also useful to determine that any anesthetics that are going to be administered do not interfere with any of the physiological parameters that are being measured (e.g., when methoxyflurane is metabolized it produces fluoride ions which may cause renal damage (Flecknell, 1987)).

In the second part of the strategy, the remaining R--replacement--is considered. There may be some overlap with the first part of the search, in that alternative animal models may already be in hand. If not, then alternative mammalian and nonmammalian models should be considered. Table 2 is a short list of useful terms that AWIC staff use. The ? is a truncation code used by Dialog. For a more complete listing, see *Searching Agricola for Animal Welfare* (Clingerman et al, 1990) and *Animal Welfare Information Center Scope Notes* (Swanson, 1991). Both are available from AWIC.

Table 2. Selected Alternatives Keywords

animal model(s)	amphibian?, reptile?	euthanas?
animal testing	simulat? (simulation(s),	handl? (handling)
alternative(s)	simulator(s))	housing, facilit?, caging
alternative(s)	computer(s)	train?, educat?, teach?
artificial	software	welfare, pain, stress,
vitro(method, model,	interactive	distress
technique)	digital image?	assay?, technique?,
culture (cell, tissue,	virtual (surgery, reality)	method?
organ)	video? (disc, display)	environ? enrich?, toy,
isolated (cell, tissue,	mannequin? (manikin)	toys, play?
organ)	mathematical model(s)	behav? enrich?
model?	cadaver?	<b>Note:</b> Refinement alternatives are found using terms relevant to the area of study.
plastinat?	anesthe?, anasthe?,	
single-celled organism?	anaesthe?	
bacteria?, protozoa?	analges?, sedative,	
invertebrate?	anxiolytic	
fish?, cephalopod?		

### WHAT IS MISSING?

Earlier in this discussion, it was noted that the phrase *animal testing alternatives* is used as an indexing term by AGRICOLA, MEDLINE, and other databases but fails to retrieve much useful information. Why? If the author of a scientific paper has not made it excruciatingly clear that the paper discusses an alternative technique or model, the indexer usually does not have the leeway to add the alternatives tag as a descriptor, keyword, or MESH term. Similarly, in looking for animal models, many authors fail to mention the species or strain of animal in the abstract or keywords. Abstracts often don't mention anesthetics, analgesics, or sex of animals used. Consequently, this information does not make it into the database. Many authors do not even mention this type of information in the body of the paper. Papers often don't mention the husbandry and environmental conditions under which the animals are kept nor are problems encountered during the course of an experiment spelled out. This is the type of information that other scientists can use to avoid the same

mistakes and thus refine a procedure or find an alternative model. A very good accounting of how scientists can improve scientific writing and add to the body of literature on alternatives can be found in Morton (1992). To ensure that articles are properly indexed, authors should include relevant alternatives terminology in the title, abstract, and keywords.

Another aspect of scientific publishing is the publishing of negative results or experiments that fail to confirm a hypothesis. While it may not seem useful at the time, the chances are very good that someone else is going to encounter the same problem. Make it known! Similarly, from personal experience, laboratories conduct small pilot studies or experiments to determine things such as the effects on receptor function or density of using carbon dioxide as a pre-decapitation anesthetic. These studies may not warrant a peer-reviewed article but may be useful as a technical note or newsletter item. The point is to make that information available. The *Animal Welfare Information Center Newsletter* welcomes articles detailing this type of information.

Finally, one of the major problems in retrieving information on alternatives is the lack of standard indexing terminology. While recognizing the importance of proprietary indexing systems to the identity and profitability of commercial databases, it would enhance information retrieval if databases could develop controlled vocabulary for alternatives terminology.

In an era when there is instant access to literally millions of scientific documents, taking the time to properly write up research will ensure that it is more easily retrieved and more widely cited.

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NAL call number: Z7994.L3A5.  
Descriptors: animal testing alternatives, cosmetics, European Union regulations, product development, animal welfare, eyes, skin, laboratory animals, mutagenicity, injection, European Union.
- Bowd, A.D. (1994). **The role of animal care committees in fostering use of alternatives: A case study.** *In Vitro Toxicology* 7(2): 169.  
Descriptors: committees, alternatives to animal testing.
- Dawson, M. (1996). **Guidelines for the choice of an alternative to proposed animal experiments.** *Developments in Biological Standardization* 86: 329.  
Descriptors: animal testing alternatives, animal welfare, Great Britain, licensing.
- Gettings, S.D., D.M. Bagley, M. Chudkowski, J.L. Demetrullas, L.C. Dipasquale, C. L. Galli, R. Gay, K.L. Hintze, J. Janus, and K.D. Marenus (1992). **Development of potential alternatives to the Draize eye test: the CTFA evaluation of alternatives program. Phase II. Review of materials and methods.** *Alternatives to Laboratory Animals: ATLA* 20 (1): 164-171.  
NAL call number: Z7994.L3A5.  
The CTFA Evaluation of Alternatives Program is a multi-year effort, organised by the CTFA Animal Welfare Task Force, designed to evaluate the performance of currently promising in vitro (alternative) methods to the Draize eye irritancy test. The sole criterion for inclusion of a particular test is that it shows some initial promise as an alternative to the Draize eye test, and that it is under evaluation or development by a participating CTFA member company. Tests are evaluated for their ability to rank and discriminate the ocular irritation potential of prototype cosmetic and personal care formulations compared to the Draize eye test. Test materials and in vitro methods currently under evaluation in Phase II of the CTFA Program are described. Additional tests may be included in subsequent phases of the Program, should it be determined that they show particular promise as replacements for specific types of



formulation. Conversely (at the discretion of sponsors), tests may be removed from the Program should initial promise be unfulfilled.

Descriptors: animal testing alternatives, evaluation, organizations.

Hart, L.A. (1995). **The animal subjects protocol process: Applying the 3Rs.** *Lab Animal* 24(5): 40-43.

NAL call number: QL55 A1L33

Descriptors: protocol preparation, protocol review, investigator's responsibilities, IACUC responsibilities, importance of animal wellbeing, alternatives, reducing sources of discomfort, approaches for the investigator, review of the literature, literature searching.

Hem, A., A.J. Smith, and P. Solberg (1998). **Saphenous vein puncture for blood sampling of the mouse, rat, hamster, gerbil, guineapig, ferret and mink.** *Laboratory Animals* 32(4): 364-368. This technique may be viewed at

[http://www.uib.no/vivariet/mou\\_blood/Blood\\_coll\\_mice\\_.html](http://www.uib.no/vivariet/mou_blood/Blood_coll_mice_.html)

NAL call number: QL55 A1L3

Descriptors: blood collection, techniques, animal welfare, alternatives to retroorbital bleeding.

Hendriksen, C.F. (1996). **A short history of the use of animals in vaccine development and quality control.** *Developments in Biological Standardization* 86: 3-10.

AB- Man has been using animals since early times to gain an insight into health, illness and death. The oldest known medical standard work, the Corpus Hippocraticum (circa 350 BC), contains descriptions of experiments on pigs. Although the first attempt at immunoprophylaxis dates as far back as the 6th century (variola was practised in China to protect people against smallpox), it was not until the middle of the 19th century that animal experimentation acquired full scientific status in the development and quality control of immunobiological products. It was Louis Pasteur and Robert Koch who, through studies on animals, succeeded in underpinning the causal relationship between infectious diseases and micro-organisms, thus opening the way to the discovery of effective therapeutic and prophylactic agents for a number of these diseases. In several respects, the experimental animal work carried out in the last decade of the 19th century to find an effective and reliable way of treating and preventing diphtheria determined the use of animals. Many common routine animal tests in the quality control of immunobiologicals arose from diphtheria research. Conversely, diphtheria was one of the first diseases where experimental animal research laid the foundation for effectively reducing child mortality. This had a very profound impact on the attitude of society towards animal experiments in those days and almost completely eliminated the growing influence of the antivivisection movement. The interest in the possibilities of replacement, reduction and refinement (the Three-Rs concept) of the use of laboratory animals is increasing for several reasons, including concern about animal welfare. The root of animal welfare can be traced back to the 18th century with the formulation of utilitarian ethics. One characteristic feature of these ethics was that the interests of any creature which is submitted to any procedure should be taken into consideration. This presentation sets out some major historical contributions of animal experiments to the development and quality control of immunobiologicals. Attention is also paid to the changing attitude of society towards animal experiments and its impact on the development of alternative methods. It is concluded that, although animal experiments have played an important part, a new area is now beginning in which increasing emphasis will be placed on in vitro methods.

Descriptors: animal welfare, diphtheria, poliovirus vaccine, quality control, animal testing alternatives.

Holden, F. (1997). **Alternatives committee established at Indiana.** *The Johns Hopkins Center for Alternatives to Animal Testing Newsletter* 14(3): 6-7.

NAL call number: HV4701 J6

Descriptors: subcommittee to IACUC, communications between researchers and campus animal protectionists, monthly round table, institutional support at highest levels, membership includes—information specialists, public relations/education representative, departmental representatives, IACUC liaison, animal protectionist, veterinarian, research assistant.

Huggins, J. (1998). **Co-occurring words: finding information about alternatives to animal testing.** *ATLA-Alternatives to Laboratory Animals* 26(6): 849-856.

NAL call number: Z7994 L3A5

Descriptors: databases, indexing, skin, literature searching, utilization of terms which co-occur can enhance information retrieval, toxicology, scientific methods, endpoints measured, informatics research.

Huggins, J. (1997). **Communication by keywords: Sharing information about alternatives to animal testing.** *Animal Welfare Information Center Newsletter* 8(2): 9-11.

NAL call number: aHV4701

Descriptors: stresses need for defined vocabulary for alternatives to animal testing, need for scientists to incorporate keywords about the methods used during experiments, toxicology, endpoints, keywords for alternatives to skin irritation.

Irwin, M.H., R.J. Moffatt, and C.A. Pinkert (1996). **Identification of transgenic mice by PCR analysis of saliva.** *Nature Biotechnology* 14(September):1146-1148.

NAL call number: QH442 B5

Descriptors: alternative to surgically obtaining samples, nested primers, gene integration, DNA purification.

Jackson, L.R., L.J. Trudel, and N.S. Lipman (1999). **Small-scale monoclonal antibody production in vitro: methods and resources.** *Lab Animal* 28(3):

NAL call number: QL55 A1L33

AB- Monoclonal antibodies (MAbs) are valuable research tools; however, MAb production via the mouse ascites method has come under recent scrutiny, due to the pain and distress it may cause the animal. The authors present a review of in vitro production of MAbs, as well as critical considerations in selecting the appropriate technique.

Jackson M.R. (1998). **Priorities in the development of alternative methodologies in the pharmaceutical industry.** *Archives of Toxicology* 20(suppl): 61-70.

NAL call number: RA1190 A7

AB-Promotion of animal welfare is an underlying and laudable goal for toxicologists and there is good reason to adopt practical, focused, investigative approaches towards this aim. Pharmaceutical regulatory toxicology can be subdivided into the areas of systemic (target organ), reproductive, genetic and topical toxicology, as well as immunotoxicology and oncology. These areas can be assessed for prioritisation as to where adoption of measures to promote any or all of the 3 Rs (reduction, replacement, refinement) would lead to the most tangible benefit for animals. These measures can range, for example, from replacement of animal experimentation with alternative in vitro techniques, to adoption of regulatory protocols that reduce the number of animals required. This paper is confined to consideration of in vitro technology in terms of reducing/replacing laboratory animal use, and a suggested list of criteria for prioritisation is potential for:- Regulatory acceptability Reducing development cost Reducing animal numbers Promoting welfare aspects Elucidating toxic mechanisms Usefulness in compound selection Advancing the science of toxicology Clear messages emerge from such an



analysis which could influence prioritisation of the application of in vitro toxicology from the standpoints of animal welfare, feasibility and resources.

Descriptors: alternatives, animal welfare, drug industry, toxicology methods, drug approval, drug screening, Great Britain.

Jennings, M., G.R. Batchelor, P.F. Brain, A. Dick, H. Elliot, R.J. Francis, R.C. Hubrecht, J.L. Hurst, D.B. Morton, A.G. Peters, R. Raymond, G.D. Sales, C.M. Sherwin, and C. West (1998).

**Refining rodent husbandry: the mouse. Report of the rodent refinement working party.** *Laboratory Animals* 32(3): 233-259.

NAL call number: QL55 A1L3

Descriptors: animal husbandry, laboratory animals, animal welfare; animal housing, hygiene, mice.

Jennings, V.M. (1995). **Review of selected adjuvants used in antibody production.** *ILAR Journal* 37 (3): 119-124.

NAL call number: QL55.A1I43.

Descriptors: adjuvants, immunostimulants, antibodies, biological production, toxicity, adverse effects, pain, granuloma, arthritis, animal welfare, laboratory animals.

Johns Hopkins University Center for Alternatives to Animal Testing (CAAT) (1997). **Alternatives in monoclonal antibody production Technical Report No. 8.** Baltimore: CAAT, 41 p.

Available from [http://altweb.jhsph.edu/~caat/pubs/tech\\_reports/techreport08.htm](http://altweb.jhsph.edu/~caat/pubs/tech_reports/techreport08.htm)

Descriptors: overview, hollow fiber reactors, comparison of in vitro and in vivo techniques, cost comparisons, quality comparisons, quantity comparisons, core laboratories, regulatory issues, European perspective, IACUC responsibilities, recommendations.

Johns Hopkins University, School of Hygiene and Public Health (1992). ***Animal Care and Use Committees and Alternatives, a Symposium Sponsored by the Johns Hopkins School of Hygiene and Public Health, Office for Research Subjects, June 18, 1992.*** Baltimore, Maryland: Johns Hopkins University, 110 p.

NAL call number: HV4704.A53 1992.

Descriptors: animal welfare, alternatives to animal testing, laboratory animals..

Kirchain, S. and R.P. Marini (1998). **A tissue harvesting program as a method for implementing the 3Rs of biomedical research.** *Lab Animal* 27(8): 37-39.

NAL call number: QL55 A1L33

Descriptors: reducing animal use, alternatives to animal testing, centralized database, information includes protocols, species, tissue donations and requests, sample forms, administration, IACUC approval, adoption program.

Koeter, H.B.W.M. (1993). **The science and the art of regulatory toxicology: how to deal with alternative tests.** In *Current Trends: in vitro skin toxicology and eye irritancy testing: proceedings of the symposium, April 21-23, 1993, Radisson Hotel, Ottawa, Ontario, Canada*, Ottawa : Joseph F. Morgan Research Foundation, p. 15-22.

NAL call number: RA1199.4.I5C87 1993.

Descriptors: animal testing alternatives, toxicology, regulations, guidelines, animal welfare.

Kreger, M.D. (1999). **The literature search for alternatives.** In *The Care and Feeding of an IACUC: The Organization and Management of an Institutional Animal Care and Use Committee*, M.L. Podolsky and V.S. Lukas, eds., Boca Raton, FL: CRC Press:, pp. 139-152. AB- Describes the process of developing and executing a multidatabase literature search for alternatives.

Descriptors: alternatives, databases, literature search, evaluation, IACUC protocol.

- Kreger, M.D. (1997). **Why conduct literature searches for alternatives?** *ASLAP Newsletter (American Society of Laboratory Animal Practitioners)* 30(3):19-23.  
NAL call number: QL55 S97  
AB- Describes the legal, ethical, and practical rationale for running a multidatabase search for alternatives. Explains the usefulness of the search and gives tips to reduce online fees.  
Descriptors: literature search, Policy 12, Animal Welfare Act.
- Langley, G., C. Broadhead, K. Bottrill, R. Combes, R. Ewbank, P. Hawkins, R. Hubrecht, M. Jennings, C. Newman, S. Rowe, J. Southtree, M. Todd, and L. Ward (1999). **Accessing information on the reduction, refinement, and replacement of animal experiments.** *ATLA-Alternatives to Laboratory Animals* 27(2): 239-245.  
NAL call number: Z7994 L3A5  
Descriptors: European regulations, information resources, problems with current resources, databases, websites, proposed solutions, recommendations.
- Leenaars, P.P.A.M., M.A. Koedam, P.W. Wester, V. Baumans, E. Claassen, and C.F.M. Hendriksen (1998). **Assessment of side effects induced by injection of different adjuvant/antigen combinations in rabbits and mice.** *Laboratory Animals* 32(4): 387-406.  
NAL call number: QL55 A1L3  
AB- We evaluated the side effects induced by injection of Freund's adjuvant (FA) and alternative adjuvants combined with different antigens. Rabbits and mice were injected subcutaneously, intramuscularly (rabbits) and intraperitoneally (mice) with different adjuvants (FA, Specol, RIBI, TiterMax, Montanide ISA50) in combination with several types of antigens (synthetic peptides, autoantigen, glycolipid, protein, mycoplasma or viruses). The effects of treatment on the animals' well-being were assessed by clinical and behavioural changes (POT and LABORAS assays) and gross and histopathological changes. In rabbits, treatment did not appear to induce acute or prolonged pain and distress. Mice showed behavioural changes immediately after (predominantly secondary) immunization. Injection of several adjuvant/antigen mixtures resulted in severe pathological changes, depending on adjuvant, type of antigen, animal species used and route of injection. Both rabbits and mice showed pathological changes ranging from marked to severe after injection of FA, and ranging from minimal to marked after Specol and Montanide injections. Pathological changes after RIBI injections were severe in rabbits, though slight in mice. After TiterMax injections, pathological changes were moderate in rabbits, though severe in mice. In conclusion, injection of FA according to present guidelines resulted mostly in severe pathological changes, whereas only very few clinical and behavioural signs indicated prolonged severe pain. Our findings indicate that Montanide ISA50 and Specol induce acceptable antibody titres, and cause fewer pathological changes than FA. Thus they are effective alternatives to FA.
- Leeuw, W.A.de, P. de Greeve, H. Schoffl, H. Spielmann, and H.A. Tritthart (1997). **Experience with the Dutch Code of Practice for the immunization of laboratory animals.** *Ersatz- und Ergänzungsmethoden zu Tierversuchen: Forschung ohne Tierversuche 1996. Fourth Austrian International Congress on Replacement and Alternative Methods for Laboratory Animals in Biomedical Science, 24-26 September 1995, University of Linz. Wien, Austria: Springer-Verlag Wien*, pp.210-217.  
NAL call number: HV4913 F672 1997  
Descriptors: laboratory animals, immunization, ethics, animal welfare, monoclonal antibodies, alternatives to animal testing, Netherlands.
- Martin, B.J., J.B. Watkins, 3<sup>rd</sup>, and J. Ramsey (1998). **Venipuncture in the medical physiology laboratory.** *American Journal of Physiology* 274(6 Pt 2): S62-7.  
AB- Medical physiology laboratories, traditionally devoted to animal experimentation, face unprecedented difficulties linked to cost, staffing, instrumentation, and the use of animals. At



the same time, laboratory experiences with living creatures play a unique role in medical education. In this article we describe the use of venipuncture and subsequent blood analysis, with medical students serving as both subjects and experimenters, in a sequence of first-year physiology laboratories. These experiments are safe, robust, inexpensive, and time efficient, and they teach the principles of cardiovascular, respiratory, renal, nutritional, and gastrointestinal physiology. In addition, they enhance medical education in several other important dimensions. First, they teach safe venous blood collection and handling, a training appropriate for students at this level. Second, by serving each week as subjects as well as experimenters, students experience aspects of both sides of the doctor-patient relationship. Third, the laboratories can be used to teach fundamentals of research design and analysis. Finally, because blood analysis is central to medicine, and because the student's own blood data are discussed, students are enthusiastic and cooperative, and the clinical relevance of the data is clear.

Descriptors: medical education, phlebotomy, physiology education, technology, medical laboratory education, glucose tolerance test, hematocrit, hemoglobins-analysis, hemostasis-physiology, kidney-physiology, metabolism-physiology, nutrition, respiration-physiology, teaching.

McArdle, J. (1998). **Alternatives to ascites production of monoclonal antibodies.** *Animal Welfare Information Center Newsletter* 8(3-4): 1-2, 15-18.

NAL call number: aHV4701 A9522

Descriptors: ascites, monoclonal antibodies, laboratory animals, animal welfare, methods, mice.

Morton, D.B. (1998). **The importance of non-statistical design in refining animal experiments.** *ANZCCART News* 11(2): 1-12 (Insert).

NAL call number: SF405.5 A3

Descriptors: laboratory animals, animal experiments, animal welfare, ethics, pain, experimental design.

Orlans, F.B. (1996). **The three Rs in the research and education: a long road ahead in the United States.** *Alternatives to Laboratory Animals: ATLA* 24 (2): 151-158.

NAL call number: Z7994.L3A5.

AB- Attitudes toward the Three Rs concept of refinement, reduction and replacement in the United States in research and education are widely divergent. Positive responses have come from several sources, notably from four centres established to disseminate information about alternatives. Funding sources to support work in the Three Rs have proliferated. The activities of institutional oversight committees have resulted in the nationwide implementation of important refinements. In the field of education, student projects involving pain or death for sentient animals have declined, and the right of students to object to participation in animal experiments on ethical grounds has been widely established. However, there is still a long way to go. Resistance to alternatives is deep-seated within several of the scientific disciplines most closely associated with animal research. The response of the National Institutes of Health to potentially important Congressional directives on the Three Rs has been unsatisfactory. The prestigious National Association of Biology Teachers, which at first endorsed the use of alternatives in education, later rescinded this policy, because of opposition to it. An impediment to progress is the extreme polarisation of viewpoints between the biomedical community and the animal protectionists.

Descriptors: animal testing alternatives, animal experiments, education, animal welfare.

Pakes, S.P. (1990). **Contributions of the laboratory animal veterinarian to refining animal experiments in toxicology.** *Fundamentals of Applied Toxicology* 15(1): 17-24.

Descriptors: animal pain, psychology, measurement, research design, alternatives, trends, veterinarians, ACUC.

Pavletic, M.M., A. Schwartz, J. Berg, D. Knapp (1994). **An assessment of the outcome of the alternative medical and surgical laboratory program at Tufts University [School of Veterinary Medicine].** *Journal of the American Veterinary Medical Association* 205(1): 97-100.

Descriptors: animal welfare, cadavers, dogs, euthanasia, veterinary education, alternatives.

Purchase, I.F., P.A. Botham, L.H. Bruner, O.P. Flint, J.M. Frazier, and W.S. Stokes (1998).

**Workshop overview: scientific and regulatory challenges for the reduction, refinement, and replacement of animals in toxicity testing.** *Toxicology Science* 43(2): 86-101.

AB- Public concern for animal welfare has been expressed through legislative control of animal use for experimental purposes since the first legislation was introduced in 1876 in the United Kingdom. Legislative control of animal use has been introduced in virtually every developed country, with major initiatives in Europe (1986) and the United States (1966 and 1985). Advances in scientific thinking resulted in the development of the concept of the three Rs--refinement, reduction, and replacement--by Russell and Burch in 1959. The field has expanded substantially since, with specialist scientific journals dedicated to alternatives, World Congresses organized to discuss the scientific and philosophical issues, and European and U.S. validation organizations being launched. Current scientific attention is focused on validation of alternative methods. The underlying scientific principles of chemical toxicity are complicated and insufficiently understood for alternative methods for all toxicity endpoints of importance in protecting human health to be available. Important lessons have been learned about how to validate methods, including the need to have prediction models available before the validation is undertaken, the need to understand the variability of the animal-based data which is to be used as the validation standard, and the need to have well-managed validation programs. Future progress will depend on the development of novel methods, which can now be validated through international collaborative efforts.

Descriptors: animal testing, alternatives, regulations, legislation, education, Europe, Great Britain, United States reproducibility of results, toxicology.

Ray, S. (1998). **An alternative to water deprivation techniques in animal learning studies.**

*Animal Technology* 49(3): 113-120.

NAL call number: QL55 I5

AB- Many laboratories use a period of water deprivation to motivate animals on a variety of water reinforced learning paradigms including aversive conditioning and maze learning tasks. Such procedures can lead to long periods without water and increase inter-animal variability in learning performance. Reported is an alternative procedure using sucrose rich drinks, or sucrose solutions, as a reward in maze and discrimination learning procedures with no prior water deprivation.

An initial experiment compares performance over trials of a water deprived group of rats learning to negotiate a Y maze, and a group of genetically matched animals running an identical maze with no water deprivation. Both groups negotiating the maze for a sucrose reward. Results show that non-deprived animals showed teaming that was equally as good as the water deprived animals. Similar results were confirmed in a Lashley jump stand discrimination task. The ability to study learning in non-deprived animals may be of great interest in studies of learned behaviour after lesion or other surgical interventions, when periods of dehydration may affect the animal's health. Further, the development of non-deprivation motivated techniques will reduce the severity of many commonly employed rodent learning paradigms.

These results may also offer a useful heuristic to explore learning paradigms without food or water deprivation schedules in other species.



Rowan, A.N. (1995). **The third R: refinement.** *Alternatives to Laboratory Animals: ATLA* 23(3): 332-346.

NAL call number: Z7994.L3A5.

AB- This review attempts to provide an introduction to the complicated subject of refinement, the third R in the concept of alternatives. It starts with a brief discussion of what refinement means and the lack of specific attention paid to this third R. This is followed by an analysis of the conceptual underpinnings of pain, distress and suffering, and the problems of both definition and measurement which must be faced if we are to be objective and consistent in our search for refinement. The review then touches upon husbandry, care and handling issues as they affect animal discomfort and distress. Antibody production, both polyclonal and monoclonal, is discussed as an example of the refinement of research techniques. Finally, a few brief comments are offered on the refinement of a variety of other experimental techniques, including those used in toxicology, cancer research and behavioural research.

Descriptors: animal experiments, pain, anxiety, stress factors, animal welfare, mice, inflammation.

Schwetz, B and D. Gaylor (1998). **Alternative tests: carcinogenesis as an example.** *Environmental Health Perspective* 106(Suppl 2): 467-71.

NAL call number: RA565 A1E54 v.106 suppl.2

AB-Acceptance of new tests that are alternatives to currently used toxicology tests is a topic of considerable importance in the field of toxicology. Carcinogenicity testing today normally includes 2-year studies in rats and mice of both sexes, following widely accepted procedures for husbandry; selection of dose levels; pathology and toxicity observations; and statistical interpretation of tumor data. These studies are usually preceded by tests for genetic toxicity and subchronic toxicity studies to select dose levels for the 2-year studies. Although these data are used for quantitative risk assessment, the mechanistic basis for effects is usually unknown. The series of studies is very expensive and requires 5 years or more to conduct. Alternative approaches are being developed that would provide more mechanistic information and hopefully would permit decisions to be made about carcinogenic potential without the need to conduct 2-year studies in rats and mice of both sexes. Decisions could be based on a profile of data rather than on the result of one test. Procedures for regulatory acceptance of new approaches for carcinogenicity testing are critical to future progress.

Descriptors: alternatives, carcinogenicity tests, methods, toxicity, animal welfare, decision making, government, mice, public policy, rats, research design, trends, time factors.

***Selection and use of replacement methods in animal experimentation.*** (1998). Herts, UK:

Universities Federation for Animal Welfare, 32 p.

Copies are available from: FRAME, Russell and Burch House, 96-98 North Sherwood Street, Nottingham NG1 4EE, UK, tel: +44 0115 958 4740, fax: +44 0115 950 3570, email:

[frame@frame-uk.demon.co.uk](mailto:frame@frame-uk.demon.co.uk)

<http://www.frame-uk.demon.co.uk> or UFAW, The Old School, Brewhouse Hill,

Wheathampstead, Herts AL4 8AN, UK, tel: +44 0158 283 1818, fax: +44 0158 283 1414, e-mail: [ufaw@ufaw.org.uk](mailto:ufaw@ufaw.org.uk) <http://www.ufaw3.dircon.co.uk>

Descriptors: legislative requirements (UK), introduction to the 3Rs, improved use of information, physical and chemical methods, mathematical and computer models, SAR, in vitro techniques, lower organisms, human tissues and volunteers, sources of tissues, sources of information, organizations, databases, on-line services.

Smaje, L.H., J.A. Smith, R.D. Combes, R. Ewbank, -R., J.A. Gregory, -J.A., M. Jennings, G.J. Moore, and D.B. Morton (1998). **Advancing refinement of laboratory animal use.** *Laboratory Animals* 32(2): 137-142.

NAL call number: QL55.A1L3

AB- Whatever view is taken of the morality of using animals in scientific research and safety testing, it can generally be agreed that so long as such use continues, every effort should be made to keep animal suffering to a minimum. This is the thinking behind the 'Three Rs' of refinement, reduction and replacement of laboratory animal use. This paper concerns refinement. We recognize that the Three Rs are taken very seriously in many countries of the world [see for example a recent editorial in the journal *Science* (Goldberg et al. 1996)] and, although we have written this paper from our own perspective in the UK, its principles are generally applicable.

Snow, B. (1990). **On-line searching for alternatives to animal testing.** *Online* (July): 94-97.  
NAL call number: QA76.55 O6  
Descriptors: developing search strategies, boolean operators, databases, category codes, terminology.

Stokes, W.S. and D.J.B. Jensen (1995). **Guidelines for institutional animal care and use committees: consideration of alternatives.** *Contemporary Topics in Laboratory Animal Science* 34 (3):51-55, 58-60.  
NAL call number: SF405.5.A23.  
Descriptors: animal testing alternatives, committees, guidelines, information services, training, regulations.

Van der Kamp, M.D.O. (1994). **Ways of replacing, reducing, or refining the use of animals in the quality control of veterinary vaccines.** Lelystad, The Netherlands: Instituut voor Veehouderij en Diergezondheid, 107 p.  
NAL call number: HV4915 K36 1994  
Descriptors: overview of veterinary vaccines, quality control, regulatory climate, alternatives to animal testing, feasibility of alternatives, recommendations.

Zeller, W., H. Weber, B. Panoussis, T. Burge, and R. Bergmann (1998). **Refinement of blood sampling from the sublingual vein of rats.** *Laboratory Animals* 32(4): 369-376.  
NAL call number: QL55 A1L3  
Descriptors: blood sampling, stress, laboratory animals, blood specimen collection, animal welfare, pain.

Zutphen, L.F.M. van and M. Balls (eds.) (1997). **Animal alternatives, welfare, and ethics, Proceedings of the 2nd World Congress on Alternatives and Animal Use in the Life Sciences, held in Utrecht, the Netherlands, 20-24 October 1996** Amsterdam, New York : Elsevier, 1260 p.  
NAL call number: QL1.D48 v.27.  
Descriptors: alternatives to animal testing, animal experimentation, animal welfare, laboratory animals, databases, literature searching.

Zutphen, B.F.M. van and J.B.F. van der Valk (1995). **Education and training: a basis for the introduction of the three Rs alternatives into animal research.** *Alternatives to Laboratory Animals: ATLA* 23(1): 123-127.  
NAL call number: Z7994.L3A5.  
AB- Education is a highly effective way of promoting the introduction of alternatives into the everyday practice of biomedical research and testing. In some countries, specific requirement for the education of persons involved in animal experimentation have been made compulsory by law. In The Netherlands, young scientists must take a course on laboratory animal science as part of, or in addition to, their biomedical graduate programme. This course provides information on the proper design of animal experiments, but also covers alternatives animal welfare issues and ethical aspects of animal experimentation. The Three RB of Russell & Burch are the guiding principles of the course, during which participants are challenged to



seek methods or techniques that can replace, reduce or refine the use of animals. Since 1985 more than 2500 people in The Netherlands have taken the course, and evaluations have indicated that a large majority of the participants appreciated this education as a contribution to both the quality of experiments and the welfare of the animals, and considered the course to be indispensable for those who are responsible for the design and performance of animal experiments.

Descriptors: animal testing alternatives, animal experiments, educational courses, training, laboratory animals, animal husbandry.

## **Useful World Wide Web sites**

### **Altweb**

<http://altweb.jhsph.edu/index.html>

A site for news, information, discussion, and resources from the field of alternatives to animal testing. This site is a collaborative effort funded by the Alternatives Research & Development Foundation, the Doerenkamp-Zbinden Foundation, the Humane Society of the United States, the Office for Protection from Research Risks at the National Institutes of Health, and the Procter & Gamble Company. It is being developed by the Center for Alternatives to Animal Testing at Johns Hopkins University, in collaboration with the Altweb Project Team (which includes AWIC), to serve academic, industrial and government scientists, educators, the media, and the general public.

### **Animal Welfare Information Center**

<http://www.nal.usda.gov/awic/alternatives/alternat.htm>

Articles and other resources concerning alternatives

### **Association of Veterinarians for Animal Rights**

<http://www.avar.org>

This site will give you access to Alternatives in Education Database, a comprehensive listing of videos, computer simulations, and other media that can be incorporated into educational curricula from high school on through medical, veterinary, or graduate school..

### **Center for Alternatives to Animal Testing (CAAT)**

<http://www.jhsph.edu/~caat/caat.html>

The Johns Hopkins Center for Alternatives to Animal Testing (CAAT) is a global resource for the development of replacement, reduction and refinement alternatives for research and testing.

### **ECVAM : European Centre for the Validation of Alternative Methods**

<http://www.jrc.it/ei/ecvam/index.asp>

Validating methods and strategies to reduce or replace the use of live animals in laboratory studies.

### **Fund for the Replacement of Animals in Medical Education**

<http://www.frame-uk.demon.co.uk/alternat.htm>

A brief survey of some ways in which the use of animals in science may be refined, reduced or replaced.

### **Guide to Searching for Alternatives to the Use of Laboratory Animals**

<http://www.frame-uk.demon.co.uk/guide/index.htm>

This guide assumes no previous knowledge of search techniques nor of the facilities available for obtaining information from the Internet.

### **ICCVAM: Interagency Coordinating Committee for the Validation of Alternative Methods**

<http://iccvam.niehs.nih.gov/>

ICCVAM and its supporting center, NICEATM (the National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods), coordinate the development, validation, acceptance, and harmonization of alternative toxicological test methods throughout the U.S. Federal government. Another great resource provided by the U.S. Government.

**The Netherlands Centre Alternatives to Animal Use**

<http://www.pdk.dgk.ruu.nl/nca.dir/>

The Netherlands Centre Alternatives to Animal (NCA) is the central point in the Netherlands for coordinating research and disseminating information on alternatives to animal experiments. One of its important tasks is to support the Alternatives to Animal Experiments Platform, in which the Dutch government, industry, and animal protection organizations collaborate.

**The Norwegian Reference Centre for Laboratory Animal Science & Alternatives**

**Knutepunktet for forsøksdyrlære og alternativer til dyreforsøk**

<http://oslovet.veths.no/>

Links to the Norina database (Norwegian Inventory of Audiovisuals (NORINA)

<http://oslovet.veths.no/NORINA>) of alternatives and other alternatives databases

**University of California Center for Animal Alternatives**

[http://www.vetmed.ucdavis.edu/Animal\\_Alternatives/main.htm](http://www.vetmed.ucdavis.edu/Animal_Alternatives/main.htm)

The Center places special emphasis on disseminating information concerning models, computer programs, and other animal alternatives in education through every level of public and private education.



# **Selected Animal Welfare Issues**







# The Science of Animal Well-being

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[Editor's Note - The following article is from the keynote address presented at the combined meeting of the American Society of Animal Science and the International Society for Applied Ethology, held in Pittsburgh, Pennsylvania, on August 8-11, 1992.]

Ladies and Gentlemen, it is a great pleasure and privilege for me to address you this evening. I want to spend my time trying to convince you that ethology the study of animal behavior is science. It uses the scientific method, and it is a branch of science that can really contribute to animal production.

It should be remembered that ethology is a very young science. Ethology came of age in 1973 when Karl von Frisch, Konrad Lorenz, and Niko Tinbergen were awarded the Nobel Prize for Medicine or Physiology. Ethology, therefore, is still in its infancy and many mechanisms remain to be elucidated. Even with further knowledge, the possibility of modeling behavior in terms of input-output equations, such as has been done in nutrition and environmental physiology, seems remote.

Let me change tack for a minute and pose this question which I lifted from an advertisement for a recently published book "What is the most complex material object in the universe?" The answer: "Your brain!" It has been calculated that the human brain contains 1011 neurons, that there are 103 synapses per neuron, and that there are 2 states per synapse. This means that the total number of possible brain states is  $2 \times 10^{14}$ ! And that is the reason why it is unrealistic to expect nice clean-cut models of behavior; the enormous complexity of the organ underlying behavior, the central nervous system, precludes it.

Of course the brain is not just an amorphous mass of neurons; it is organized, and is a system of specialized subsystems. However, even simplified interactional models of brain function (e.g., Bindra, 1976) show that it is extremely complex.

At this combined meeting of the American Society of Animal Science and the International Society for Applied Ethology, there will be many papers dealing with animal behavior. I would like to whet your appetite by describing very briefly three examples of excellent applied behavioral research. They are particularly interesting because of the implications of the results for other branches of animal science.

My first example concerns the research of Ian Taylor who did his graduate work at the University of Illinois. Ian (Taylor et al., 1988) did a very thorough survey of feeders for sows and found that they were very inefficient. This resulted in large amounts of food being spilled and also in injuries to the animals using the feeders. Ian then filmed at high speed the heads of sows as they were feeding in an unencumbered situation. He then very carefully analyzed the film frame by frame

and digitized the positions of certain key anatomical features. This allowed him to calculate the envelope of space that the sow requires as she feeds.

Ian went on to design a sow feeder (and other swine feeders, using similar methods) based on the information gained from the behavioral observations. These feeders waste 0.5 percent of food compared to the traditional range of wastage of 2-17 percent. Consider the improvement to productivity of this sort of saving achieved simply through careful observation of how animals behave. These improved feeders also do not injure the animals.

My second example is the work of Temple Grandin (Grandin, 1983) who designs handling facilities for animals. Her cattle-handling facilities are based on a fundamental knowledge of animal behavior. The visual field of the species involved, the flight distance of animals, what they perceive as frightening, the angle at which they move away from a frightening stimulus these and many more factors go into designing this sort of facility. The benefits are enormous: the whole unit works more smoothly and efficiently, the quality of meat is higher, and the downgrading is less. All this through the application of fundamental principles of animal behavior.

My third example is taken from the work of Anne Marie de Passille. Anne Marie has been doing some intensive research on sucking behavior in calves, and I wish to describe just one small part of her work (de Passille et al., 1991). The calves are kept in individual pens and fed a set amount of milk from buckets. Immediately after feeding, one group is allowed to suck on solid rubber teats for a few minutes. This results in an increase in the levels of several of the digestive hormones such as insulin, gastrin, and cholecystokinin. We often see examples of hormones' driving behavior - but here it is the performance of the behavior that is affecting the hormones. The implications are that we may get a more efficient digestive process by allowing calves to suck even if it is non-nutritive sucking. And this is quite apart from any welfare implications.

I hope that these three examples have shown you that there are a variety of ways in which studies of behavior can have beneficial application in animal production. In connection with Anne Marie's research, I mentioned animal welfare, and I now wish to talk about that in more detail.

### **Problem 1 - What is animal welfare?**

Some time ago, Marian Dawkins and I suggested that it was impossible to give "animal welfare" a precise scientific definition. We thought that a loose working definition would be one that encompassed the ideas of the animal in mental and physical health, the animal in harmony with its environment, the animal being able to adapt to its environment without suffering and that we should also take the animal's feelings into account (Duncan and Dawkins, 1983). A loose working definition of "suffering" is a wide range of unpleasant emotional states.

More recently, the idea has emerged that welfare is mainly (Dawkins, 1990) or solely (Duncan and Petherick, 1989, 1991) dependent on what the animal feels.

Scientific evidence on the welfare of farm livestock is urgently required so that rational decisions can be made on intensive production systems and practices. Many different classes of evidence have been investigated with a view to identifying reliable indicators of reduced welfare. Productivity indicators have proved unreliable, and biochemical and physiological indicators have not lived up to their early promise. There has, therefore, been increasing interest in the use of behavior to assess welfare. The idea of being able to assess the welfare of animals by looking at their behavior is an appealing one: the technique is non-invasive, it could be available in the field without specialized equipment, it might give an instantaneous indication of welfare, and behavioral changes might precede some of the other indicators of reduced welfare.

## **Problem 2 - Welfare involves science, ethics, and aesthetics.**

We need to acknowledge that welfare problems can be only partially solved by scientific answers. Once the facts are known, society also needs guidance in making ethical decisions. There is probably no difficulty if it is shown, say, that a husbandry system leads to a great deal of distress. However, there will be many cases in which there are both welfare costs and benefits to the animal, and these will be problematical. It is also likely that aesthetic judgments enter into the decision making process. Thus, I think that it offends some people aesthetically to see cattle kept in feedlots without access to grazing and chickens kept in cages, no matter what science has to say about animal welfare under these conditions.

## **Problem 3 - How can welfare be assessed?**

I would now like to lead you through three examples of ways in which behavior has been used to assess the welfare of poultry.

### **Case 1 There has been a general criticism voiced that "Hens in battery cages will be frustrated." How can this be investigated scientifically?**

Many years ago, I set out to investigate this question. The approach I took was to subject chickens experimentally to many different frustrating situations and to make a list of all the behavioral responses that they showed (Duncan, 1970). I frustrated the birds' tendencies to feed, to nest, to behave sexually, to incubate eggs, and to brood chicks in many different ways. The behavioral responses that the birds made were very limited. Hens which were mildly frustrated experimentally showed an increase in displacement preening (Duncan and Wood-Gush, 1972a). If the frustration was severe, they showed stereotyped back-and-forward pacing (Duncan and Wood-Gush, 1972b). If two or more birds were frustrated simultaneously, the dominant birds showed an increase in aggression towards the subordinates (Duncan and Wood-Gush, 1971). There was also evidence that severe frustration was very aversive to the birds (Duncan and Wood-Gush, 1974). Rather surprisingly, the symptoms of severe frustration, stereotyped back-and-forward pacing, and increased aggression, with one exception, are not commonly seen in battery cages. It can be concluded that, generally speaking, caging per se does not lead to severe frustration. Displacement preening is seen in battery cages, which suggests that a state of mild frustration is fairly common under commercial conditions. However, it is also commonly seen under natural conditions and seems to be the birds' way of responding to everyday problems.

The exception mentioned above is that certain strains of hens in battery cages show stereotyped back-and-forward pacing (Wood-Gush, 1972) and increased aggression (Hughes, 1979) during the prelaying phase when they appear to be frustrated because they cannot find a suitable nest site.

From these results, I would argue that the main cause of reduced welfare in battery cages is frustrated nesting behavior. There is now some intensive research going on in the U.K., both at Bristol and Edinburgh, to try to incorporate a nesting site or sites into the battery cage.

### **Case 2 Feather pecking and cannibalism have been problems in poultry production for many years. The industry's solution is to de-beak or beak-trim the birds. Is this a problem for the birds?**

There is no doubt that an outbreak of feather pecking and cannibalism in a group of chickens greatly reduces their welfare. The injuries inflicted can be horrific and can lead to death. The procedure called de-beaking or beak-trimming, in which about a third of the upper beak and a small part of the lower beak are removed with a sharp heated blade, is very effective in preventing the



worst of the damage. It would, therefore, seem that there are great welfare benefits to be gained from this procedure. However, there is now good morphological, neurophysiological, and behavioral evidence that beak trimming leads to both acute and chronic pain. The morphological evidence is that the tip of the beak is richly innervated and has nociceptors or pain receptors (Breward, 1984). This means that cutting and heating the beak will lead to acute pain. In addition, it has been shown that as the nerve fibers in the amputated stump of the beak start to regenerate into the damaged tissue, neuromas form (Breward and Gentle, 1985). Neuromas are tiny tangled nerve masses that have been implicated in phantom limb pain (a type of chronic pain) in human beings. The neurophysiological evidence is that there are abnormal afferent nerve discharges in fibers running from the amputated stump for many weeks after beak trimming long after the healing process has occurred (Breward and Gentle, 1985). This is similar to what happens in human amputees who suffer from phantom limb pain. The behavioral evidence is that the behavior of beak-trimmed birds is radically altered for many weeks compared to that which occurs immediately before the operation and compared to that shown by sham-operated control birds. In particular, classes of behavior involving the beak, namely feeding, drinking, preening and pecking at the environment, occur much less frequently, and two behavior patterns, standing idle and dozing, occur much more frequently. The only reasonable explanation of these changes is that the birds are suffering from chronic pain (Duncan et al., 1989).

These facts taken together provide strong evidence that beak trimming is not such a trivial operation as has previously been thought. It almost certainly causes both acute and chronic pain. There is, therefore, a welfare cost as well as a benefit in carrying out this procedure. The same may hold true for other surgical interventions that are commonly practiced in animal agriculture, such as tail-docking, castration, de-horning, etc. Many of these are carried out for welfare reasons, e.g., sheep are commonly tail-docked to prevent blow fly strike, a condition that reduces welfare enormously and causes high mortality. However, it is seldom acknowledged that there may be a welfare cost to the animal. There may be all sorts of welfare costs apart from acute and chronic pain. To continue with the tail-docking example, the animals may be frightened by the procedure, there may be a social cost (perhaps because they cannot signal to each other so effectively), or they may be frustrated (because they cannot flick flies away).

I am suggesting that some sort of cost-benefit analysis should be carried out on these procedures. This will not be easy. Cost-benefit analysis is anything but an exact science. Ernst Schumacher in his seminal book *Small Is Beautiful*, was very disparaging about cost-benefit analysis. He said, Cost/benefit analysis is a procedure by which the higher is reduced to the level of the lower and the priceless is given a price. It can, therefore, never serve to clarify the situation and lead to an enlightened decision. All it can do is lead to self-deception or the deception of others; for to undertake to measure the immeasurable is absurd and constitutes but an elaborate method of moving from preconceived notions to foregone conclusions; all one has to do to obtain the desired results is to impute suitable values to the immeasurable costs and benefits (Schumacher, 1973). I am not as negative as Schumacher but I do realize that there are difficulties in making such an analysis. However, if we do not admit that these routine surgical procedures have costs and at least attempt the exercise, then we will continue to deceive ourselves. Perhaps the exercise of acknowledging that there are costs will be sufficient incentive to look for alternative solutions.

### **Case 3 Do hens in battery cages "miss" items like a dust bath, a foraging substrate, a sexual partner, etc?**

In asking these questions, we are really trying to "get inside the head" of the animals. We are trying to find out "how they feel" about what we are doing to them. Of course, subjective feelings are not directly accessible to scientific investigation. In the case of human beings, it is possible to find out indirectly how they feel by asking them, but how can we find out how an animal feels? Fortunately, in the welfare debate, it is not necessary to know exactly how an animal feels; even an indirect

measure of feelings, such as how positive or negative these feelings are, would be extremely helpful. Perhaps animals could tell us how they feel by what they choose; they might vote with their feet. This rationale forms the basis of preference testing, which has been used extensively in poultry science (Duncan, 1992). In a preference test, the animal is given a choice between certain aspects of its environment and it is assumed that it will choose according to how it feels, i.e., in the best interests of its welfare.

However, there are certain pitfalls that have to be guarded against when using preference tests (discussed in more detail by Duncan, 1992). When designing preference tests for animals, we must also ensure that the choices made are not trivial. Likewise, we must ensure that in a preference study the animal is not choosing the lesser of two evils. If we know what the pitfalls are, then we can take suitable precautions to avoid them.

One of the ways in which the strength of preference can be measured is by finding out how hard the animal will work to gain access to its preferred choice. We have borrowed a variety of obstructive techniques from the psychology laboratory to find out how important to the animal its choices are (Duncan and Kite, 1987). In these tests, the animal is taught to walk in a runway towards the putative reward, which might be food, a dust-bath, a companion, etc. Various obstructions, such as a weighted push-door, are then placed in the runway between the animal and the "reward," and we can see how hard the animal will work to reach the goal (Petherick et al., 1990).

I hope I have convinced you that animal welfare can be better understood (and therefore improved) by a rational scientific approach. An understanding of behavior is going to play a crucial role. I can assure you that the animal welfare issue (a) will not disappear, and (b) cannot be solved by public relations work alone. There is a danger that if this nettle is not grasped, animal agriculture will be seen as ethically challenged or morally handicapped.

The question can then be asked "Do we have the necessary expertise working on this topic?" I have tried to assemble some figures, compiled from organizational directories, for a few Western countries. Figure 1 shows the number of applied ethologists working full time with agricultural species in the United States, Canada, the United Kingdom, Denmark, and the Netherlands at the end of 1991. I have tried to be as evenhanded as possible, but these numbers should only be considered approximate. They show that each of these countries has about 10-11 applied ethologists working with agricultural species, apart from the U.K. which has about twice that number. However, when these numbers are expressed according to the value of the livestock industry, a rather different picture emerges. In Figure 2, I have shown the same numbers expressed according to \$1 billion (U.S.) farm cash receipts for animals and animal products generated during 1991.

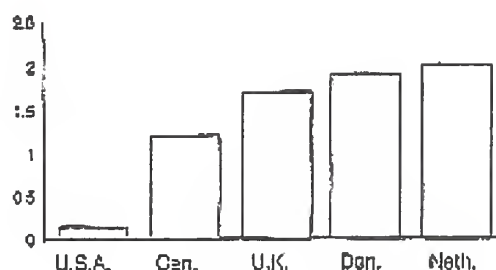
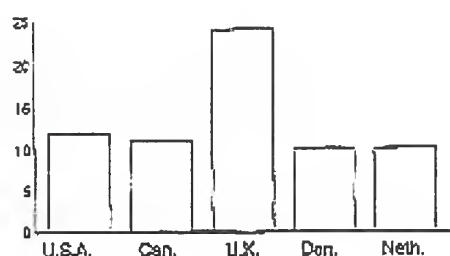


Fig. 1 (left) Number of applied ethologists working with agricultural species in 1991.

Fig. 2 (right) Number of applied ethologists per value of livestock industry (per \$1 billion farm cash receipts generated in 1991).



Once again these numbers should only be considered approximate. It now appears that the United States has a much lower research effort going into this area, only a tenth of the effort being expended by some European countries.

I would like to finish up with a quotation from one of my favorite poets, the Irishman W.B. Yeats. In his poem, *An Irish Airman Foresees His Death*, Yeats says:

I balanced all, brought all to mind,  
The years to come seemed waste of breath,  
A waste of breath the years behind  
In balance with this life, this death.

To me, this summarizes the quintessential human characteristic. Human beings can contemplate past events. They can look into the future and foresee their own death. They can make a balance. I believe that this is the "morally relevant difference" between human beings and animals which the animal rights movements fail to acknowledge. There is evidence that animals can feel pain, and I think we have a moral responsibility to eliminate or reduce pain in our animals. There is evidence that animals can feel frightened and frustrated, and I think we have an obligation to reduce these states of suffering as much as possible. However, there is no evidence that animals have any concept of their own mortality. Let me tell you that if I thought they did, I would become a vegetarian tomorrow. I believe that this is the unique human quality.

However, it brings with it a grave responsibility. It means that we have to make decisions, we have to make the balance, we have to carry out the audit, for the animals in our charge. I am optimistic. I think that we can do it. But we will only do it reasonably and rationally and defensibly, if first we carefully gather the scientific evidence.

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# Arguments for Single-caging of Rhesus Macaques: Are They Justified?

by

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Human primates are social by nature and strive best in the supportive environment of compatible conspecifics. Being forcefully deprived of companionship is therefore one of the most dreaded punishments. Nonhuman primates share the same basic "social needs" (36) as human primates do, and sociality is central to their very survival (2). Like human primates, nonhuman primates may become mentally disturbed when chronically kept in social isolation, and they often express their distress in abnormal behavior patterns (cf. 6).

Despite the inherent ethical problems related to social deprivation, social housing of nonhuman primates is seen as a husbandry priority only by a minority of primatological investigators (14). Thus, single-caging is still the prevailing housing condition for laboratory primates (13, 30). The regulatory "safeguard" (15) prescribing social housing (36) is apparently not very effective. The following arguments are often brought forward in justification of the traditional single-caging:

1. The animals are too aggressive to be socialized with each other.
2. Socially housed animals are at greater health risk than individually housed animals. They suffer distress from being constantly exposed to companionship. Subordinate animals become undernourished because of food competition.
3. Pair-housed animals become bored of one another.
4. Social-housing interferes with research protocols.

The present paper examines the justification of these notions as they pertain to the most common laboratory nonhuman primates, i.e., rhesus macaques (*Macaca mulatta*).

Numerous studies have indeed shown that unlike in other nonhuman primate species (e.g., *Pan troglodytes*, 7; *Cebus apella*, 1; *Saimiri sciureus*, 12) group formation and subsequent group-housing of rhesus macaques is likely to be associated with serious problems related to aggressive intolerance (e.g., 5, 10). Alternative pair formation and subsequent pairhousing techniques have therefore been developed for rhesus macaques (17, 18, 21, 4) in order to avoid the risk attendant on group-housing. How successful are these techniques?

- No noteworthy aggression was observed when either 64 or 104 juveniles were transferred from single-caging to heterosexual and isosexual pair-housing conditions for one year (33, 31).

- Transferring 65 adult females and 13 adult males from single- to pair-housing arrangements with infants for one year was successful in 93 percent of cases (94 percent of female/infant pairs, 92 percent of male/infant pairs). Pairs were split due to aggression in 3 percent of cases. Inadequate food sharing and 'teasing' accounted for the other 4 percent of pair incompatibility (31).

- Transferring 154 adult females and 40 adult males from single-caging to continuous isosexual pair-housing conditions with each other for one year was successful in 87 percent of cases (88 percent of female pairs, 80 percent of male pairs). Partners were separated in 6 percent of cases because one of them seriously aggressed the other. Inadequate food sharing or depression accounted for the remaining 7 percent of partner incompatibility (31).

- Transferring 24 previously single-caged adults of both sexes to uninterrupted isosexual pair-housing conditions for three to seven years was associated with pair incompatibility in 12

percent of cases, with serious aggression accounting for 3 percent. There were no indications that long-term compatibility of male pairs was less than that of female pairs, that partners did not readily adjust to new companions, or that the presence of offspring jeopardized the compatibility of companions (32).



Photo by V. Reinhardt

These findings indicate that "the conventional wisdom that unfamiliar adult macaques are more likely to fight than to coexist peacefully" (11) does not hold true for the most common and, supposedly, most aggressive species, i.e., *Macaca mulatta*. The published information available provides evidence that no unreasonable risk of aggressive intolerance accrue when previously single-caged individuals are subjected to careful pair-formation and subsequent permanent pair-housing protocols (c.f. 27). Pair-housing effectively avoids the typical aggression problems of group-housing.

The health risk associated with pair-housing as compared to conventional single-housing was assessed in three independent studies. In no case was clinical morbidity, as measured in rate of veterinary treatment, higher in pair-housed than in single-housed subjects (23, 4, 35). In a study of 96 monkeys transferred from single- to compatible pair-housing conditions, subjects required veterinary treatment once every 909 days while singly caged, versus once every 2,104 days while pair-housed (35). This suggests that pair-housing may be an effective housing strategy not only from the behavioral but also from the veterinary point of view (35).

Three separate investigations examined the stress status of compatible pair-housed versus single-housed animals. Serum cortisol concentrations (26, 33) and immune stress response (4) of subjects did not differ in both housing conditions. Stress indices of subordinate animals were not higher than those of their dominant partners (26, 4).

Rather than being a source of distress, the compatible companion may function as a source of security (e.g., 8). This is particularly relevant for the experimental context in which the presence of a familiar conspecific functions as a buffer against environmental stress that the single-caged individual is lacking (21). Needless to say that scientific data collected from such a 'stress-protected' subject are less confounded than data collected from a socially deprived research subject (cf. 3). The comforting rather than distressing effect of companionship can also be inferred from the fact that individuals afflicted with gross behavioral disorders often abandon their neurotic activities after being provided with a compatible cage mate (18, 19, 11).

Three independent studies failed to find a negative impact of pair-housing on body weight development (20, 29, 4). There was also no evidence found of dominant animals gaining more body weight than their subordinate partners (20, 4). This is not surprising because adequate food sharing is an important condition to qualify a pair as compatible and allow partners to stay together (22).

The stimulatory effect of a cage mate has been evaluated in animals that have lived together as pairs for one year or longer. Five investigations have shown that paired companions spend approximately the same amount of time interacting with each other in species-typical ways (figure 1) as do wild animals living in troops (16, 24, 29, 4, 34). This suggests that a compatible cage mate--unlike inanimate toys--maintains its stimulatory effect over time, probably because of its inherent ever-changing nature.



It has been documented that the following research-related procedures can readily be accomplished in pair-housed rhesus macaques:

- capture from cage (28);
- blood collection in the subject's home cage (25);
- tethering (25); and
- headcap implantation (22, 25).

Procedures such as controlled food intake, and urine and fecal sampling require the temporary separation of partners with transparent cage dividing panels, allowing uninterrupted visual, olfactory, and auditory contact.

The findings presented in this report indicate that common arguments in justification of the traditional single-caging of rhesus macaques are often based on subjective assumptions rather than on scientific facts. Providing the animals a social environment in the form of compatible pair-housing arrangements does not unduly jeopardize their safety (no conspicuous aggression problems), health (no conspicuous veterinary problems), physical well-being (no signs of distress), behavioral well-being (species-typical expression of social needs; amelioration of behavioral disorders) and adequate food intake, nor does it interfere with common research procedures. Professional standards stipulate that "unless absolutely essential, primates should not be housed alone in a cage on a long term basis" (9). The question of what makes it "absolutely essential" to deprive the majority of research rhesus macaques of social contact and social interaction by housing them permanently alone in single cages remains to be answered.

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# Adoption of Research Animals

by

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Estimates of actual numbers of research animals used in the country vary, but one thing is obvious to most of us working in research facilities: the vast majority of these animals are euthanized when their usefulness has ended. Euthanasia is intrinsic to some projects. For example, many projects, especially those using the smaller laboratory animals, require the euthanasia of the animal for tissue collection. Other projects may lead to illness or disease conditions for which euthanasia is the most humane treatment. Often, however, animals finish a research project in good health and yet may not be suitable for any other research projects at the institution. There may be overstock from a breeding colony, with no research use for some of the young animals produced. In these circumstances, people will naturally consider the possibility of finding adoptive homes for the animals.

It seems that research workers, especially the technicians, students, and veterinarians who work most directly with the animals, have a real emotional need to see some animals escape the system, to break free of the research laboratory. If we defend animal research by claiming that we only use, harm, or kill research animals when necessary, then it follows that we will want to do our best to ensure good lives for those animals whose sacrifice is not required by our science. Arnold Arluke has described the tendency of laboratory workers to occasionally single out individual animals as laboratory pets, animals who stay in the research facility, but are elevated in status, treated as individual companions, and spared use in experimentation, if possible (Arluke 1993).

Recently, Jan Wyrich has described the adoption program for research animals at the University of California, San Francisco (Wyrich 1996). She observes that an adoption program can decrease stress and raise morale for both the research and the animal care teams and bring both groups to a greater mutual appreciation in the process.

Why discuss adoption in a newsletter devoted primarily to alternatives and the three Rs of replacement, refinement, and reduction? Adoption typically happens *after* a research project ends and does not obviously affect the numbers of animals used; it does not result in their replacement with nonsentient alternatives. Both the Animal Welfare Act regulations and the *Guide for the Care and Use of Laboratory Animals* are silent on the topic. Adoption programs may count as refinements, alternative endings to the story. Most people working in research laboratories see the value of humane and painless euthanasia for animals who are suffering. They may accept that healthy animals must often be killed in the course of a study. Killing healthy animals when there is no research need, however, feels wrong to many of us, especially when a viable adoptive home is available.

Adoption considerations need not happen only after termination of a project. More and more I see researchers designing projects with adoption in mind, choosing experimental endpoints and final data collection with the dual goals of valid data and a group of young, healthy animals ready for adoption. They may hire student workers to help socialize the animals and start to spread the word among the staff early in the project that a particular group of animals will be available for adoption.

As more data are collected on the success or failure of different programs, researchers may base their choice of animal breed, age, sex or housing in part on considerations of adoptability.

Some people may resist the idea of adoption. They will point to the fact that these animals are not pets, they were bred for research, as if that fact alone should dictate their fates after the research has ended. Perhaps in our drive to give research animals the best possible lives, we are uncomfortable admitting that life in a laboratory for many species is still a pale comparison to life with a loving family. Adoption programs also undermine any complacency we may have that euthanasia, competently and painlessly performed, is no real harm or injustice to the animals. And adoption programs carry heavy costs, both in money and labor, that someone at the institution must bear.

Virtually any species of research animal may be considered for adoption. With dogs and cats in particular, adoption may be driven by the research and animal care teams, which know that animals that are no longer needed for their project are healthy and of good temperament. In these cases, the staff may actively search for adoptive homes for the animals, spreading the information by word of mouth, posters, or e-mail. Potential owners may be on-campus staff or students or off-campus. Some breeding colonies will even maintain a waiting list of potential homes.

With other species of animals, the more usual adoption route seems to be that an individual worker or student becomes attached to a particular animal and wants to take it home. Individual rats, rabbits, frogs, goats, or various other animals may be selected for adoption even when there is no drive to find homes for every animal on the project. When this happens, seemingly more adoptable animals may be left behind while the quirky individual-- the sickly one, the runt, the escape artist, the "talker"-- finds a new home.

Sharon Matter has reviewed some of the many arguments for and against the adoption of research animals (Matter 1996). Human health and safety are major concerns, and with them, institutional liability if the adopter gets sick or injured. Most snakes, frogs, and other ectotherms are *Salmonella* suspects, even if there has been no positive culture. Many dogs carry ascarids, *Giardia*, and other potentially zoonotic infections. Dogs, cats, or other animals may bite their adoptive owner or children in the house. Institutions need to devise ways to minimize risks, to inform new owners of persistent risks, and to discourage legal action should human illness or injury occur. Signed release forms are part of this effort, though they have limited legal standing in most States.

It is impossible to reduce risk to zero. No live animal can be guaranteed not to bite or scratch. Finances will limit the number of zoonotic infections that can be screened for, and the screening tests themselves have limited sensitivity. Institutions need to decide what level of risk is acceptable and how to inform owners explicitly of potential problems.

A visible adoption program can broadcast the message that the institution conducts animal research. It is difficult to maintain a closed-door policy or to tightly monitor public relations when research animals are at large in the community. "I had no idea your university uses so many dogs," is the sort of statement we may not want to hear. However, if the person saying that is driving home with her healthy new pet, that may be just the public relations effort research institutions need. Students, technicians, and others who see healthy animals euthanized when the administration forbids adoption will feel little compunction to keep their disapproval to themselves for long.

Running an adoption program is time consuming and costly, as our Nation's animal shelters can attest. A research institution may feel more pressure than would a humane shelter to run diagnostic testing for zoonotic infections, to fully vaccinate adoptive research animals, and to spay or neuter them. There may be interviews with the potential adopters to ensure that the animal is going to a good home. The University of California at San Francisco (UCSF) estimates an average of almost



\$300 per animal in staff time and supplies is spent preparing animals for transfer to local humane shelters for adoption (Wyrich 1996b). In describing an adoption program for University of Pennsylvania beagles, Harry Ake details a program with heavy time demands on laboratory animal veterinarians, interviewing potential adopters, filling out paperwork, and examining the dogs (Ake 1996). Some of these duties can be delegated to technicians, students, or even volunteers; others, such as rabies vaccination, surgical neutering, and health certificates, cannot.

Animal welfare questions are a top concern. How well does a dog that has been kennelled all her life adapt to life in a home? Can the institution effectively screen potential homes? Do we really even know what makes a good adoptive home? What will become of animals if the adoption fails? A research institution's adoption program can potentially compete with neighboring animal shelters' programs. Some animal protectionists have argued against research animal adoption, at least while shelters are over-burdened with adoptable animals, and for the way it assuages our consciences, as researchers, about killing animals. With this avenue for guilt avoidance, the pressure to truly reduce the numbers of animals we use in laboratories may be lessened.

Adoption programs vary. UCSF has an active and conscientious program that is unusual in its close association with local cooperating humane shelters (Wyrich 1996). As an alternative to direct adoption, most UCSF animals are sent to one of two local shelters for adoption. Most institutions seem to restrict themselves to direct adoption with no such middle man. A recent survey of Institutional Animal Care and Use Committee (IACUC) policies revealed that only 20 percent of institutions surveyed report allowing any of their research animals to be adopted (Borkowski 1995). I do wonder how many animal adoptions happen at the other 80 percent, unbeknownst to the officials running the IACUC and responding to the survey.

Unfortunately, all this work is done with little data to support specific policy recommendations. Wyrich describes the UCSF adoption program as successful, but does not provide her criteria for this assessment. Over 500 animals have found adoptive homes since 1982, with no major repercussions to the university (Wyrich 1996). That certainly sounds successful, but offers little guidance on which aspects of the program explain this success. At an average cost of \$300 per adoption, one wonders whether a program at half that cost could be equally successful.

Harry Ake answers more specific questions in his follow-up survey of beagle adoptions from the University of Pennsylvania. Ake tabulates adopters' assessments of their feelings about their new dogs and whether they would recommend similar adoptions to others (Ake 1996). House-breaking stands out as a key issue for pet adopters in this survey. We have a similar adoption follow-up survey in progress at Cornell University with a more heterogeneous population of dogs. Our preliminary data reveal a similar concern among owners for house-soiling beagles, unfortunately, performing worse in this category than either golden or Labrador retrievers. This breed difference in behavior has been identified in the general pet population as well (Hart and Miller 1985). The age at adoption also seems to influence a dog's chance of remaining with his or her adoptive owners in our own survey and in Patronek's survey of risk factors for surrender of animals to humane shelters (Patronek 1995).

In both the Cornell and University of Pennsylvania surveys, over 80 percent of dogs were still with their adoptive owners several months after adoption (of course, neither survey had a 100-percent response rate). Is 80 percent a good success rate? Currently, there are few comparative data on the success of adoption of animals from other sources such as pet stores or shelters.

Owner satisfaction varies as much with the owner as with the animal. I know of one veterinary student, for instance, who crated her 9-year-old adoptive laboratory beagle for over a year before she could trust her loose in the house without soiling. But she loved her little beagle, her Newfoundland played with it, as did her adopted research cat, and the foursome made for a happy household. Other



owners would not have tolerated such a long housebreaking period and would have reported an unsuccessful or short-lived adoption.

Neither our Cornell survey nor Ake's Pennsylvania survey have identified owner characteristics or behaviors that are predictive of successful adoption. Ake and Matter discuss screening or interviewing potential owners but give no criteria. Again, data are sparse. Surveys at Purdue of people surrendering animals to shelters suggest that certain owner behaviors such as taking a new dog to obedience training or to a veterinarian are in some way associated with higher numbers of owners retaining their adopted or purchased dogs (Patronek 1995). I have worried that owners who adopt research animals under pressure to save the animal's life would not make strong and lasting bonds; these fears have so far not been confirmed.

In conducting these surveys, we do not hope to distinguish successful from unsuccessful adoptions or to formulate a blanket policy for or against the practice. Rather, we hope that adoption is a policy that institutions will consider and that we can identify potential problems to be remedied and strategies to be used. As more data are gathered, we will be able to generate a profile of the ideal adoption candidate. We also hope to counsel and support owners and their pets during the early months of home life while the family bond develops.

For institutions that are thinking about allowing adoptions, here are some considerations:

**1) *Legal and administrative.*** Institutional attorneys should help to draft a good release form that the new owner signs. Animals are adopted as is, with no guarantee that they are housebroken, will stay healthy, or are not carrying some potentially zoonotic infections. Proper documentation and USDA forms must be filed.

Decide on what sort of follow-up support you are willing and able to give such as behavior consultations, vaccines and veterinary advice, or taking the animal back if the adoption is unsuccessful. Often the adoption process is driven by the most junior staff and students. Faculty and the administration may be permissive but not highly supportive. Senior level administration must be aware and in support of the program, as there will inevitably be problems that they must deal with. Staff time, husbandry supplies, and diagnostic testing take resources as the adoption program grows. The level of commitment the institution has to the adoption program will determine where these resources come from and how carefully animals are screened before they leave the institution.

**2) *Choose the animals carefully.*** Hard luck cases have enormous appeal to some people and may be appropriate for some carefully selected owners. Animals with visible defects that are retired from surgical projects, for instance, are conspicuous reminders of their research or teaching origins. Will the new owner explain this to others in a way that your institution finds acceptable? Animals on infectious disease studies, especially with zoonotic infections, are rarely acceptable adoption candidates. Large dogs of questionable temperament are not good adoption candidates. My preference is that food animal species be retired as pets, not as breeders or meat. Few of the drugs and anesthetics they will have received have been cleared for use in animals intended for human consumption. Agriculture programs that raise animals for research and sale are the exception to this rule, but antibody-production rabbits and goats or fetal-catheterization sheep, for instance, should be retired only as pets.

**3) *Work with local humane societies.*** You may not have direct cooperation with your local shelter, but they should know about your program. Many research animals are tattooed. These animals may find their way to the local shelter either as lost animals or as unsuccessful adoptions. The shelter will want to contact someone at the institution with the tattoo number and get complete information on the animal's history. This also gives the institution some feedback on their adoption policy.

**4) Practice the Three R's.** Institutions can reduce the number of surplus animals in need of homes by coordinating different lab groups for tissue collection and by planning breeding colonies to meet research demands without overproduction. A well-coordinated and well-informed laboratory animal resources department can help balance two potentially competing goals: conservation by channeling animals from one project to another (typically, terminal) project versus placing animals in adoptive homes. Training and socialization are further refinements that can help dogs and cats thrive in the laboratory and in adoptive homes. Survey data show that if the laboratory dog is housebroken while at the institution, the adoption is more likely to be satisfactory and long-lasting. Volunteers might be employed to teach dogs who are available for adoption some basic house manners.

**5) Expect problems.** Dogs may bite. Cats may hide under a couch for a year. Families may develop infections, and the physician suspects their pet. Animals may become ill shortly after adoption. Animals with behavior problems may end up at the local shelter. You are working to minimize the risk of unsuccessful adoption; you can only eliminate it by banning adoption altogether. Even then, problems are not entirely eradicated, as clever staff will find ways to slip their favorite animals out the back door with a wink and a nod, and a note in the record that the puppy was euthanized.

**6) Follow up on adoptions.** Thorough surveys are time-consuming research projects that not every institution will want to conduct. Data are sorely lacking to guide refinement of adoption programs, however, and more information is needed. If the institution does not actively solicit information on adoption success, only the failures will be known, whether they are brought back to the institution or surrendered to a local shelter. The successful adoptions remain invisible to the institution in most cases, even though they appear to predominate by a healthy margin.

Adoption programs for research animals can boost employee morale, enhance public relations, and most importantly, give research animals a chance to find a loving home. They do require work, time, and money. If institutions put some of the time, energy, and resources into disposition of their animals that they typically put into animal acquisition, a program that benefits everyone can be developed.

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# Oocyte Harvesting in *Xenopus laevis*

This guideline was revised and approved by the National Institutes of Health Animal Research Advisory Committee on February 10, 1999 and may be found at <http://oacu.od.nih.gov/ARAC/oocyte.htm>

Amphibian oocytes are used for studies in molecular biology, embryology and biochemistry. Stage I-VI oocytes are obtained by surgical laparotomy. Multiple surgeries on a single animal may be justified considering the reduction in the total number of animals used over the long term. However, the total number of animals used must be considered relative to the pain or distress experienced by an individual animal.

1. The total number of laparotomies should be limited and will depend on the condition of the animal and quality of the oocytes as well as the life span of the animal and the duration of egg production. Up to five recovery surgeries (the 6th would be terminal) per animal are acceptable. Additional survival surgeries should have approval of the individual ACUC.

2. Surgeries should be performed by trained personnel using appropriate anesthesia such as tricaine methane-sulfonate (MS-222). Surgeries should be done as aseptically as practical including the use of sterilized instruments and gloves.

3. Single housing or small group housing for several days after surgery should be considered as part of the post surgical care of laparotomized animals. Frogs should be monitored daily during this period for appetite as well as for any complications such as dehiscence or infection. Such adverse effects would be reasons for immediate euthanasia.

4. Adequate recovery time should be allowed between laparotomies. The investigator can alternate oocyte collection between left and right ovaries and consider rotation of frogs so that the interval between surgeries in any individual is maximized. Recovery time of less than one month should have approval of the individual ACUC.





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AB- A series of studies was undertaken to determine whether CO<sub>2</sub> can be used as a humane as well as practical agent for euthanasia or anesthesia of rats. Human volunteers rated the degree of discomfort associated with breathing 50 to 100% CO<sub>2</sub> mixed with oxygen. Increasing concentrations of CO<sub>2</sub> were judged as progressively more noxious, from "highly unpleasant" for 50% CO<sub>2</sub> to "painful" for 100% CO<sub>2</sub>. The practical aspects of anesthesia and euthanasia with 50 to 100% CO<sub>2</sub> were studied, using male Sprague Dawley rats. Time to anesthesia and death were inversely related to CO<sub>2</sub> concentration, as were the frequency and severity of adverse reactions, including seizures and hemorrhaging from the nose. The severity of edema and hemorrhage, which were observed on histologic examination of the lungs of all rats euthanized with CO<sub>2</sub>, were greatest in the animals exposed to the lowest concentrations. There were no significant effects of CO<sub>2</sub> concentration on time to recumbency or recovery, and there were no significant effects of precharging versus not precharging the chamber on any of the parameters studied. It was concluded that, although CO<sub>2</sub> can be used in a humane manner, the concentrations that are least likely to cause pain and distress are associated with the longest times to anesthesia and death, highest incidence of unwanted side effects, and most severe histologic changes in the lungs. Acceptably humane and reasonably practical euthanasia or anesthesia can be achieved using a nonprecharged chamber and a low gas flow rate so that conscious animals are never exposed to CO<sub>2</sub> concentrations >70%.

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Hammond, A.C. (1994). **Animal well-being in pharmacology and toxicology research.** *Journal of Animal Science* 72 (2): 523-527.

NAL call number: 49 J82.

AB- The primary objective of this paper is to heighten the awareness of animal welfare issues among animal scientists. Emphasis is placed on issues relating to pharmacology and toxicology research with animals. Use of both laboratory animals and farm animals is addressed; major consideration is given to domestic livestock. Animal welfare issues are complex and have philosophical, ethical, legal, societal, scientific, and biological bases and implications. There is substantial diversity in public opinion and perception regarding use of animals in research, including the belief among some people that use of animals in research should be eliminated altogether. Increasingly, public opinion is tending toward expectations of alternatives to the use of live animals for research. From an animal scientist's viewpoint, although the availability and development of viable alternatives are increasing, live animal research in pharmacology and toxicology currently has no acceptable alternative, in many cases because of the complex interactions involved in whole-animal (biological) systems. Compliance with federal, state, and local laws, regulations, and policies requires animal scientists to use only appropriate species for research, use the minimum number of animals needed, minimize pain and discomfort, and consider alternatives to the use of live animals. In summary, it is essential that animal scientists be advocates of animal well-being and adhere to appropriate guidelines for animal care and use when conducting research with animals.

Descriptors: laboratory animals, livestock, animal experiments, animal welfare, pharmacology, toxicology.

Hawkins, P. (1999). **Working together to improve rodent well-being.** *Lab Animal* 28(2):

NAL call number: QL55A1L33

Abstract: The UK has seen a productive relationship between animal welfare and research interests. This has culminated in the formation of the Royal Society for the Prevention of Cruelty to Animals/Universities Federation for Animal Welfare (RSPCA/UFAW) Rodent Welfare Group, in which technicians, researchers, veterinarians, and animal advocates share information and experience. The author provides some highlights from recent group meetings.

Hem, A., A.J. Smith, and P. Solberg (1998). **Saphenous vein puncture for blood sampling of the mouse, rat, hamster, gerbil, guinea pig, ferret and mink.** *Laboratory Animals* 32(4): 364-368.

NAL call number: QL55 A1L3

Descriptors: alternatives (to retroorbital bleeding), blood sampling techniques, laboratory animals, blood specimen collection, animal welfare.

Hendriksen, C.F.M. and W. de Leeuw (1998). **Production of monoclonal antibodies by the ascites method in laboratory animals.** *Research in Immunology* 149(6): 535-542.

NAL call number: QR180 A5

Descriptors: ascites, monoclonal antibodies, animal welfare, animal testing alternatives, production methods.

Herck, H. van, V. Baumans, C.J.W. Brandt, A.P.M. Hesp, J.H. Sturkenboom, H.A. van Lith, G. van Tintelen, and A.C. Beynen (1998). **Orbital sinus blood sampling in rats as performed by different animal technicians: The influence of technique and expertise.** *Laboratory Animals* 32 (4): 377-386.

NAL call number: QL55 A1L3



Descriptors: clinical signs, Pasteur pipette or a haematocrit capillary, lateral vs medial canthus of the orbit.

Herck, H. van, V. Baumans, N.R. van der Craats, A.P.M. Hesp, G.W. Meijer, G. van Tintelen, H.C. Walvoort, and A.C. Beynan (1992). **Histological changes in the orbital region of rats after orbital puncture.** *Laboratory Animals* 26(1): 53-58.

NAL call number: QL55 A1L3

Descriptors: retroorbital bleeding, pasteur pipette, capillary tube, hemorrhage in puncture track and periosteum, inflammation present four days after procedure in puncture track, eye muscles, periosteum and Harderian gland, no lesions detected at 28 days post-procedure, differences between techniques and technicians.

Institute Of Laboratory Animal Resources (1996). **The Psychological well-being of nonhuman primates.** Washington, DC: National Academy Press, 168 p. Full-text document is available at <http://pompeii.nap.edu/books/0309052335/html/index.html>

NAL call number: in process

Descriptors: essentials of a program to provide psychological well-being, general care, effect of special research conditions, prosimians, new world monkeys, old world monkeys, apes, research needs.

Institute Of Laboratory Animal Resources (1996). **Laboratory Animal Management Series: Rodents.** Washington, DC: National Academy Press, 167 p.

Descriptors: rats, mice, gerbils, hamsters, guinea pigs, laboratory animal management, animal husbandry, veterinary care, animal facilities, animal care.

Jackson, L.R. and J.G. Fox (1995). **Institutional policies and guidelines on adjuvants and antibody production.** *ILAR Journal* 37(3): 141-152.

NAL call number: QL55 A1I43

Descriptors: monoclonal antibody production, selection of animals, immunization protocols, priming agents, inoculation of hybridoma cells, abdominal paracentesis, clinical observations, alternatives, polyclonal antibody production, antigen preparation, antigen-adjuvant emulsions, routes, volumes, and sites of administration, post-injection observations, blood collection, restraint, institutional resources, personnel safety.

Jackson, L.R., L.J. Trudel, J.G. Fox, and N.S. Lipman (1999). **Monoclonal antibody production in murine ascites. I. Clinical and pathologic features.** *Laboratory Animal Science* 49(1): 70-80.

NAL call number: 410.9 P94

AB- BACKGROUND AND PURPOSE: Murine ascites production has been associated with appreciable morbidity and mortality, thus raising animal-welfare concerns. To address these concerns, the clinicopathologic changes associated with in vivo production of monoclonal antibodies in mice were characterized, and results were compared among cell lines. METHODS: Five hybridoma cell lines were grown in groups of 20 mice. Fourteen days prior to inoculation with 10(6) hybridoma cells, mice were primed with 0.5 ml of pristane given intraperitoneally; 12 mice were sham treated (controls). Ascites fluid was collected a maximum of three times by abdominal paracentesis. Clinical observations and pre- and postabdominal tap body weights were recorded. Necropsies were performed on all mice. RESULTS: For all groups combined, overall survival to tap 1 was 98%, to tap 2 was 96%, and to tap 3 was 79%; survival among groups ranged from 90 to 100% for tap 1, 85 to 100% for tap 2, and 35 to 100% for tap 3. Disseminated intra-abdominal seeding with irregular soft tissue and/or solid tumor masses was observed at necropsy. CONCLUSIONS: Significant clinicopathologic changes were associated with monoclonal antibody production in mice, and differences between various hybridoma cell lines were apparent.

Jennings, M, G.R. Batchelor, P.F. Brain, A. Dick, H. Elliot, R.J. Francis, R.C. Hubrecht, J.L. Hurst, D.B. Morton, A.G. Peters, R. Raymond, G.D. Sales, C.M. Sherwin, and C. West (1998).

**Refining rodent husbandry: the mouse. Report of the rodent refinement working party.** *Laboratory Animals* 32(3): 233-259.

NAL call number: QL55 A1L3

Descriptors: animal-husbandry, animal welfare, animal housing, cages, hygiene.

Ladewig, J. **Behavior of laboratory animals under unnatural conditions.** *Archives of Toxicology* 20(suppl): 41-46.

NAL call number: RA1190 A7

AB-Domestic animals are animals whose living conditions and reproduction, among other things, are controlled by man. As such, the current discussion about the welfare of domestic animals is similar for farm, companion, laboratory, and zoo animals. It concerns identification of the behavioral and physiological needs of the animals and development of living conditions that enable them to satisfy these needs. The paper describes two approaches that have been used in behavior biology to identify such needs. One approach is the measurement of stress responses that may be activated when an animal's needs are not fulfilled. The other approach is the use of operant conditioning techniques to establish demand functions by which the motivation of an animal to perform a specific behavior is measured. It is concluded that, since welfare is characterized by the absence of a number of factors, such as stress, pain, fear, disease, hunger etc., many types of measurements must be applied to ensure optimal welfare.

Descriptors: animal welfare; animal psychology, behavior, laboratory animal science.

Leenaars, P.P.A.M., M.A. Koedam, P.W. Wester, V. Baumans, E. Claassen, and C.F.M. Hendriksen (1998). **Assessment of side effects induced by injection of different adjuvant/antigen combinations in rabbits and mice.** *Laboratory Animals* 32(4): 387-406.

NAL call number: QL55 A1L3

AB- We evaluated the side effects induced by injection of Freund's adjuvant (FA) and alternative adjuvants combined with different antigens. Rabbits and mice were injected subcutaneously, intramuscularly (rabbits) and intraperitoneally (mice) with different adjuvants (FA, Specol, RIBI, TiterMax, Montanide ISA50) in combination with several types of antigens (synthetic peptides, autoantigen, glycolipid, protein, mycoplasma or viruses). The effects of treatment on the animals' well-being were assessed by clinical and behavioural changes (POT and LABORAS assays) and gross and histopathological changes. In rabbits, treatment did not appear to induce acute or prolonged pain and distress. Mice showed behavioural changes immediately after (predominantly secondary) immunization. Injection of several adjuvant/antigen mixtures resulted in severe pathological changes, depending on adjuvant, type of antigen, animal species used and route of injection. Both rabbits and mice showed pathological changes ranging from marked to severe after injection of FA, and ranging from minimal to marked after Specol and Montanide injections. Pathological changes after RIBI injections were severe in rabbits, though slight in mice. After TiterMax injections, pathological changes were moderate in rabbits, though severe in mice. In conclusion, injection of FA according to present guidelines resulted mostly in severe pathological changes, whereas only very few clinical and behavioural signs indicated prolonged severe pain. Our findings indicate that Montanide ISA50 and Specol induce acceptable antibody titres, and cause fewer pathological changes than FA. Thus they are effective alternatives to FA.

Marbrook, J. (1998). **Transgenesis and animals in research - an overview of animal welfare considerations.** *Surveillance* (Wellington, New Zealand) 25(2): 12-14.

NAL call number: SF604.63 N45S87

Descriptors: laboratory animals, animal welfare, genetics, transgenic animals.

Markowitz, H. and A. Gavazzi (1995). **Eleven principles for improving the quality of captive animal life.** *Lab Animal* 24(4): 30-33.

NAL call number: QL55 A1L33

Descriptors: ability to collect or gather food, varying food availability periodically, novelty, control of environment, socialization, continuing assessment of animals in their cages, animal caretaker interaction.

Martin, B.J. (1995). **Evaluation of hypothermia for anesthesia in reptiles and amphibians.** *ILAR Journal* 37(4): 186-190.

NAL call number: QL55 A1I43

Descriptors: research and regulatory guidelines, IACUC evaluation of hypothermia as an appropriate method, review of scientific literature, physiological changes, pathological changes, literature does not support the use of hypothermia as a clinically efficacious method of anesthesia.

McIntosh, J. and E.C. Staley (1989). **Limits of food and water deprivation.** In *Science and Animals: Addressing Contemporary Issues* H.N. Guttman, J.A. Mench, and R.C. Simmonds (eds.), Bethesda, Maryland: Scientists Center for Animal Welfare, p.117.

NAL call number: HV4704.S33 1989

Descriptors: protocol, food/water intake, controlled feeding, monitoring of animals.

Meer, M. van der, V. Baumans, and L.F.M. van Zutphen (1996). **Transgenic animals: What about their well-being?** *Scandinavian Journal of Laboratory Animal Science* 23(Suppl.1): 287-290.

NAL call number: QL55 S322

Descriptors: welfare problems may arise at many different levels—experimental procedures used to introduce DNA constructs, integration of microinjected DNA into the genome is unpredictable and may cause unintended insertional mutations, review of research.

Moberg, G.P. (1999). **When does stress become distress?** *Lab Animal* 28(4): 22-26.

NAL call number: QL55 A1L33

Descriptors: defining stress and distress in laboratory animals, stress model, perception of the stressor, biological defense, measuring stress reaction, recognizing changes in biological function, prepathological state, cumulative cost of multiple stressors, summated stressors, managing stress and distress.

Moore, C.J. and T.B. Mephram (1995). **Transgenesis and animal welfare.** *Alternatives to laboratory animals: ATLA* 23 (3):380-397.

NAL call number: Z7994 L3A5

AB- The two main techniques used in biomedical research for the production of transgenic animals have several implications for animal welfare in terms of the Three Rs of Russell & Burch. Some are intrinsic to the transgenic objectives, while others relate to the effects of mutations, transgene expression, associated methodologies, and husbandry or production systems. All of these actual and potential implications for animal welfare demand serious consideration within a broad ethical analysis of the technology. In the light of the Three Rs, this may require a fundamental reappraisal of the processes by which such scientific procedures are approved.

Descriptors: transgenic animals, gene transfer, domestic animals, animal welfare, laboratory animals, animal models, genetic effects, literature reviews.



- Morton, D.B. (1998). **Perceived and actual welfare issues - laboratory animals.** In *Ethics, welfare, law and market forces: the veterinary interface. Proceedings of a Symposium, Royal College of Veterinary Surgeons, UK, 14-15th November 1996*, A.R. Michell and R. Ewbank, (eds.), Wheathampstead, UK: Universities Federation for Animal Welfare (UFAW), p. 91-106.  
NAL call number: HV4704 E84 1998  
Descriptors: animal welfare; laboratory animals
- Niemi, S.M., J.S. Venable, and H.N. Guttman (eds.) (1994). **Rodents and Rabbits , Current Research Issues: Proceedings of a Conference Sponsored by Scientists Center for Animal Welfare (SCAW) and Working with Animals Used in Research, Drugs, and Surgery (WARDS) held in Washington, D.C. on May 21, 1993.** SCAW: Greenbelt, MD and WARDS: Fairfax, VA, 81 p.  
NAL call number: SF407.R6R63 1994.  
Contents: Request for changes in USDA regulations by Martin L. Stephens -- Recognizing stress in rodents and rabbits by Gerald F. Gebhart -- Enrichment techniques for rodents and rabbits by David Morton -- Transgenic rodents by Terrie Cunliffe-Beamer -- Anesthesia, analgesia for rodents and rabbits by Sally K. Wixson -- Aseptic surgery for rodents by Marilyn J. Brown -- Adjuvant comparison in rabbits by David K. Johnson.  
Descriptors: rodents as laboratory animals, rabbits as laboratory animals, animal experimentation, animal welfare.
- Niemi, S. (1989). **Use of immune stimulants.** In *Science and Animals: Addressing Contemporary Issues* H.N. Guttman, J.A. Mench, and R.C. Simmonds (eds.), Bethesda, Maryland: Scientists Center for Animal Welfare, pp. 119-121.  
NAL call number: HV4704.S33 1988  
Descriptors: adjuvant, ACUC, laboratory animals, ascites.
- Oestermann, D.J., J.M. Scimeca, J. Forsythe, R. Hanlon, and P. Lee (1997). **Special considerations for keeping cephalopods in laboratory facilities.** *Contemporary Topics in Laboratory Animal Science* 36(2): 89-93.  
NAL call number: SF405.5 A23  
Descriptors: biology and life history, basic tank and sea water system requirements, receiving and post-shipment handling, feeding, common health problems, health monitoring and treatment, postmortem evaluation.
- Poole, T.B. (1995). **Guidelines and legal codes for the welfare of non-human primates in biomedical research.** *Laboratory Animals* 29(3): 244-9.  
Descriptors: animal husbandry, animal welfare, housing, physiology, legislation, behavior, Canada, Europe, Great Britain, United States.
- Poole, T. (1997). **Happy animals make good science.** *Laboratory Animals* 31(2): 116-124.  
NAL call number: QL55.A1L3.  
AB- In this paper the question is posed whether it is not only better for the animal to be happy, but whether its state of mind may also have the potential to influence the scientific results derived from it. To ensure good science, the animal should have a normal physiology and behaviour, apart from specific adverse effects under investigation. There is a growing body of evidence from a wide variety of sources to show that animals whose well-being is compromised are often physiologically and immunologically abnormal and that experiments using them may reach unreliable conclusions. On scientific, as well as ethical grounds, therefore, the psychological well-being of laboratory animals should be an important concern for veterinarians, animal technicians and scientists.  
Descriptors: laboratory animals, animal welfare, immune response, handling.



**Preparation and Maintenance of Higher Mammals During Neuroscience Experiments. Report of a National Institutes of Health Workshop, March 1991.** Bethesda, Maryland: DHHS, Public Health Service, National Institutes of Health, 45 p.

NAL call number: HV4930 P74

Descriptors: prolonged non-survival recording procedures, survival anatomical procedures, perinatal procedures, inducing neurological deficits, awake behaving preparations, animal care and use concerns, sample research protocols.

Reinhardt, V. (1997). **Training nonhuman primates to cooperate during handling procedures: a review.** *Animal Technology* 48(2): 55-73.

NAL call number: QL55 I5

Descriptors: literature review, blood collection, injections, topical drug application, blood pressure measurement, urine collection, capture, minimize distress, validity of data, baboons, macaques, chimpanzees, drills, gorillas, marmosets, capuchins, vervets.

Reinhardt, V. and A. Reinhardt (1992). **Quantitatively tested environmental enrichment options for singly-caged nonhuman primates: a review.** *Humane Innovations and Alternatives* 6: 374-383.

NAL call number: QL55.H8.

Descriptors: primates, laboratory mammals, cages, environmental enrichment, psychological wellbeing, animal welfare.

Reinhardt, V., C. Liss, and C. Stevens (1996). **Space requirement stipulations for caged non-human primates in the United States: a critical review.** *Animal Welfare* 5(4): 361-372.

NAL call number: HV4701.A557.

Descriptors: primates, laboratory animals, cage size, height, space requirements, abnormal behavior, regulations, animal welfare.

Rollin, B.E. (1997). **An ethicist's commentary on the case of the infected research animal.** *Canadian Veterinary Journal* 38(3): 136.

Descriptors: rats, veterinary medicine, animal welfare, infectious disease research.

Ruiven, R. van, G.W. Meijer, A. Wiersma, V. Baumans, L.F.M. van Zutphen, and J.

Ritskes-Hoitinga (1998). **The influence of transportation stress on selected nutritional parameters to establish the necessary minimum period for adaptation in rat feeding studies.** *Laboratory Animals* 32(4): 446-456.

NAL call number: QL55 A1L3

AB- After transportation of rats by car and by air to and from the laboratory for a total period of 15 h, measurements were carried out for a period of 3 weeks after transport. Control and transported animals were housed in the same laboratory before and after transportation. During transport the animals had access to food and water. As blood collection could also cause stress, a factorial design was carried out with transport and blood collection as main factors (12 rats per group). Transport or blood collection did not cause significant effects on the following parameters: body weight, growth, clinical observation, and blood activities of lactate dehydrogenase and aspartate aminotransferase. Water intake was significantly increased after transport. Food intake did not show consistent effects after transport or blood collection. Unexpectedly, blood corticosterone levels were significantly lower in the transported animals at day 1 after transport. After 3 days these levels had returned to normal. Blood glucose, blood free fatty acids and blood urea nitrogen concentrations were incidentally decreased, whereas total cholesterol levels showed an incidental rise in the transported rats. The open-field behaviour test revealed no clear-cut results concerning the effects of transport or blood collection on faeces production, rearing and ambulation. It is concluded that after transport, an adaptation period of 3 days appears to be sufficient for rats to be used in nutritional studies.

Descriptors: adaptation, animal transport, rats, feeding studies, stress, blood collection, food intake, water intake, corticosterone, body weight, lactate dehydrogenase, aspartate aminotransferase, nutrition research.

Schlingmann, F., W.J. Pereboom, and R. Remie (1993). **The sensitivity of albino and pigmented rats to light. A mini review.** *Animal Technology* 44(2): 71-85.

NAL call number: QL55 I5

AB-Light is the most important environmental factor for animals. However, most animal facilities are designed for the convenience and comfort of the people who work in it, and not for the experimental animals. Several studies show that these light intensities are causing damage to the photoreceptor cells in the retina. Albino rats are especially more sensitive to light when compared to pigmented rats. Light values as recommended by several guidelines are often too high. Retinal degeneration seems not only to be dependent on intensity, but also on the wavelength of the light source. Finally, the role of light in the maintenance of circadian rhythm is discussed.

Smith, K.R. and R.A. Markle (1998). **Capsaicin use in neonatal rats: Husbandry and welfare concerns.** *Lab Animal* 27(10): 38-40.

NAL call number: QL55 A1L33

Descriptors: Commonly used to induce long-lasting neural desensitization in neonatal rats, clinical side-effects, initial respiratory distress, skin lesions, urine retention, considerations when employing capsaicin treatment, animals may not show signs of pain and distress due to neural insensitivity, few papers in literature describe complications, complications may have acted as a selective force on experimental animals possibly altering data.

Toth, L.A., A.W. Dunlap, G.A. Olson, and J.R. Hessler (1989). **An evaluation of distress following intraperitoneal immunization with Freund's adjuvant in mice.** *Laboratory Animal Science* 39(2): 122-126.

NAL call number: 410.9 P94

Descriptors: adverse effects, immunization, pain, stress, adjuvants, Freund's, albumin, multiple granulomatous abdominal adhesions, lymphoid hyperplasia, animals did not appear to be chronically impaired, mice.

**United Kingdom Coordinating Committee on Cancer Research guidelines for the welfare of animals in experimental neoplasia. (1989).** Institute of Laboratory Animal Resources, National Research Council. *ILAR News* 31(3): 16-21.

NAL call number: QL55.A1I43

Descriptors: laboratory animals, animal welfare, neoplasms, guidelines, United Kingdom, tumor growth.

Voipio, H-M. (1997). **How do rats react to sound?** *Scandinavian Journal of Laboratory Animal Science* 24(Suppl. 1): 1-80.

NAL call number: QL55 S322

Descriptors: Ph. D. dissertation, review of literature, ultrasonic vocalizations, vocalizations, hearing ability, physiological responses, materials and methods, sounds used in experiments, chambers, experimental procedures, behavior monitoring, response to sounds, groups, female groups, pups, comparison of sexes, statistics.

Webster, A.J.F. (1998). **The nature of physiological stress.** In *Ethics, welfare, law and market forces: the veterinary interface. Proceedings of a Symposium, Royal College of Veterinary Surgeons, UK, 14-15th November 1996*, A.R. Michell and R. Ewbank, (eds.), Wheathampstead, UK: Universities Federation for Animal Welfare (UFAW), p.177-189.

NAL call number: HV4704 E84 1998

Descriptors: animal welfare, stress, adrenal cortex hormones.

Weihe, W.H. (1998). **The impact of stress and discomfort on experimental outcome.** *Archives of Toxicology* 20(suppl): 47-59.

NAL call number: RA1190 A7

AB-Stress refers to a physiological and emotional state of man and higher animals in which the autonomic regulation is overstrained and temporarily disturbed under the impact of conflicting stimuli. Stress activates, invigorates, acts life-sustaining, and initiates and drives adaptive changes towards improved fitness. While the positive action is commonly underestimated, much attention is given to the discomfort and the strain of efforts required during coping. The label of stress as being bad and the core of suffering has been applied with particular empathy to laboratory animals, for they are kept in captivity and are exposed to experimental procedures. The husbandry conditions to which the animals are adapted are commonly standardized. This applies to procedures for subacute and chronic toxicity testing. Acute toxicity tests are the classical example of stress research in which the demands on the organism exceed the limits of its regulative capacity. Stressors are: the test compound, the procedure proper and preceding treatment of the animal. The experimental stress contributes to model the real situation. The weighting between the stressors may modify the outcome of the test.

Descriptors: animal welfare, animal psychology, laboratory animal science, stress, physiopathology, toxicology, research.

Wiepkema, P.R., W.G.P. Schouten, and P. Koene (1993). **Biological aspects of animal welfare: new perspectives.** *Journal of Agricultural & Environmental Ethics* 6 (special suppl.2): 93-103.

NAL call number: BJ52.5.J68.

Descriptors: livestock, animal welfare, stress, emotions, social interaction.

Witkin, J.M. (1989). **Issues in the use of aversive stimuli in animal experimentation.** In *Science and Animals: Addressing Contemporary Issues* H.N. Guttman, J.A. Mench, and R. C. Simmonds (eds.), Bethesda, Maryland: Scientists Center for Animal Welfare, pp. 115-116.

NAL call number: HV4704.S33 1989

Descriptors: noxious stimuli, alternatives, parameters, evaluation of proposals.

Wolfensohn, S.E. (1997). **Brief review of scientific studies of the welfare implications of transporting primates.** *Laboratory Animals* 31(4): 303-5.

NAL call number: QL55 A1L3

Descriptors: primates, psychology, stress, animal husbandry, standards, physiology, transportation.

Zeller, W., G. Meier, K. Burki, and B. Panoussis (1998). **Adverse effects of tribromoethanol as used in the production of transgenic mice.** *Laboratory Animals* 32(4): 407-413.

NAL call number: QL55 A1L3

Descriptors: anesthesia, embryo transfer, ketamine, xylazine, histopathology, animal welfare.

Zutphen, L.F.M.van and M. Balls (eds.) (1997). **Animal alternatives, welfare, and ethics, Proceedings of the 2nd World Congress on Alternatives and Animal Use in the Life Sciences, held in Utrecht, the Netherlands, 20-24 October 1996** Amsterdam, New York :Elsevier, 1260 p.

NAL call number: QL1.D48 v.27.

Descriptors: alternatives to animal testing, animal experimentation, animal welfare, laboratory animals, databases, literature searching.



# Issues in Rodent Housing

## Group vs. isolation, solid bottom vs. wire-grid bottom cages

Arnold, C.E. and D.Q. Estep (1994). **Laboratory caging preferences in golden hamsters (*Mesocricetus auratus*)**. *Laboratory Animals* 28(3): 232-238.

NAL call number: Q155 A1L3

Descriptors: hamsters, housing, behavior, flooring, litter, animal welfare, cages, wire-bottoms, solid-bottom.

Boot, R., H. van Herck, and J. van der Logt (1996). **Mutual viral and bacterial infections after housing rats of various breeders within an experimental unit**. *Laboratory Animals* 30(1): 42-45.

NAL call number: QL55 A1L3

AB-Fifteen athymic rat strains from 11 breeding colonies were housed within an experimental facility for an immunological study. Health status records supplied with 14 of the strains listed infections by Kilham's rat virus (KRV), *Clostridium piliforme* (*Bacillus piliformis*) and *Pasteurella pneumotropica* for 2, 2 and 1 colonies respectively. In sera taken previous to the study from euthymic rats of 10 strains, antibodies to KRV were detected in 3 strains, to Pneumonia virus of mice (PVM), Rat corona virus (RCV) and Sendai virus in one strain each and to *P. pneumotropica* in 2 strains. Only 2 of the KRV infections had been reported by the supplier. During the study rats of all 10 strains developed antibodies to 2-4 of viral antigens. Eight out of 10 rat strains seroconverted to 1-5 of the antigens *C. piliforme* (*B. piliformis*), *Bordetella bronchiseptica*, *Haemophilus* spp., *P. pneumotropica* and *Streptobacillus moniliformis*. Two rat strains housed in filtertop cages did not develop antibodies to bacterial antigens. The potential detrimental effects of intercurrent infections on the outcome of the comparative immunological study are discussed.

Brown, K.J. and N.E. Grunberg (1995). **Effects of housing on male and female rats: crowding stresses male but calm females**. *Physiology and Behavior* 58(6): 1085-9.

NAL call number: QP1 P4

AB-Housing conditions affect behavioral and biological responses of animals. Effects of same-sex grouped, crowded, or individually housed conditions on plasma corticosterone levels of male and female Wistar rats were examined in two experiments. Experiment 1 examined the effects of individual vs. crowded housing conditions on corticosterone, a biochemical index of stress, in seven male and seven female rats. Experiment 2 extended the findings of Experiment 1 by separately manipulating spatial and population aspects of housing with 50 male and 50 female rats. Male rats had higher corticosterone levels under crowded conditions. In contrast, female rats had higher levels when individually housed. Spatial crowding was the key variable for males, whereas the number of other animals was more important for females. These results indicate that investigators must consider housing conditions as an intervening variable that is likely to differentially affect behaviors of male and female rats.

Descriptors: behavior, housing, sex characteristics, sex differences, stress, physiopathology, analysis of variance; corticosterone, Wistar rats.

Clough, G. (1991). **Suggested guidelines for the housing and husbandry of rodents for aging studies**. *Neurobiology of Aging* 12(6): 653-8.

AB-The available published guidelines for the housing of rodents are reviewed, and assessments are made with regard to whether the data on which these guidelines are based appear to be sound. Ambient air temperature, relative humidity, lighting levels and photoperiods, sound levels, cage sizes, and ventilation rates are discussed, and a summary is provided covering the relationship



between these and other factors and the well-being of laboratory rats and mice exposed to such conditions.

Descriptors: aging physiology, animal husbandry standards, housing standards, rodents.

Everitt, J.I., P.W. Ross, and T.W. Davis (1988). **Association of wire caging with development of mouse urological syndrome.** *Laboratory Animal Science* 38(4): 507.

NAL call number: 410.9 P94

Descriptors: mice, urinary tract diseases, cages, wire-bottoms.

Hurst, J.L., C.J. Barnard, C.M. Nevison, and C.D. West (1997). **Housing and welfare in laboratory rats: welfare implications of isolation and social contact among caged males.** *Animal Welfare* 6(4): 329-347.

NAL call number: HV4701 A557

Descriptors: animal welfare, physiopathology, housing, animal behavior.

Klir, P., R. Bondy, J. Lachout, and T. Hanis T (1984). **Physiological changes in laboratory rats caused by different housing.** *Physiologia Bohemoslovaca* 33(2): 111-21

AB-Males rats of the Wistar strain (Institute of Physiology, CSAV ) were divided into six groups from the 30th to the 200th day of age. Rats (n=54) were put into cages in various numbers (1, 2, 3, 4, 6 and 8 animals in a cage) and were weighed regularly and the consumption of water and food was measured. At the end of the experiment the animals were killed and the weight of some organs and hematological values were determined. During the experiment the highest weight was attained in animals with 3 or 4 members in one cage. The differences in weight were significant from the 80th day of age. The consumption of diets and water was not influenced significantly by the number of animals in a cage. On the 200th day, the differences between the groups were found in the weight of some organs, and in some hematological values.

Descriptors: physiology, body weight, crowding, housing, rats, inbred strains, blood cell count, hematocrit, lung, organ weight, pituitary gland, testis, anatomy and histology.

Kuhnen, G. (1999). **Housing-induced changes in the febrile response of juvenile and adult golden hamsters.** *Journal of Experimental Animal Science* 39(4): 151-155.

NAL call number: QL1 J687

Descriptors: stress, body temperature, housing, animal welfare, fever, environmental enrichment, lipopolysaccharide, housing conditions significantly affect febrile response of juvenile and adults, hamsters.

Manser, C.E., H. Elliott, T.H. Morris, and D.M. Broom (1996). **The use of a novel operant test to determine the strength of preference for flooring in laboratory rats.** *Laboratory Animals* 30(1): 1-6.

NAL call number: QL55 A1L3

AB-A previous study showed that laboratory rats preferred to dwell on a solid floor rather than a grid one, particularly when resting (Manser et al. 1995). The strength of this preference was investigated in an operant trial using a novel test apparatus, which consisted of a grid-floored cage and a solid-floored cage, joined via a central box containing a barrier whose weight was adjustable. Trials in which rats had to lift the barrier in order to explore the whole apparatus were alternated with those in which the rats were confined on the grid floor and then had to lift the barrier in order to reach the solid floor. The latter trials were carried out at the beginning of the light period when the rats were seeking a resting place. In both trials, the weight of the barrier was progressively increased for each rat, until a maximum weight was found which it would lift either to explore its environment (weight A) or to reach the solid floor (weight B). No significant differences were found between weights A and B, showing that rats would work as hard to reach a solid floor to rest on as they would to explore a novel environment. The apparatus used could, with some modifications, be appropriate for use in other operant studies in laboratory rats.

Manser, C.E., T.H. Morris, and D.M. Broom (1996). **An investigation into the effects of solid or grid cage flooring on the welfare of laboratory rats.** *Laboratory Animals* 29(4): 353-363.

NAL call number: QL55 A1L3

AB-The welfare of laboratory rats housed on either solid or grid floors was investigated in several ways. No differences were found in body weight gain, food consumption or water consumption amongst rats housed in either condition. When handling was standardized between the 2 groups, there was no correlation between flooring and docility. Preference testing revealed that rats chose to dwell on solid floors rather than grids, regardless of previous housing experience. This preference for solid floors was particularly marked (88%) when the animals were resting and much less marked during activity (55.4%). Since the rats were observed to spend 70 to 75% of their time resting, it was concluded that their welfare was likely to be improved by housing them on solid floors.

Milligan, S.R., G.D. Sales, K. Khirnykh (1993). **Sound levels in rooms housing laboratory animals: an uncontrolled daily variable.** *Physiology & Behavior* 53(6): 1067-76.

NAL call number: QP1 P4

AB-High sound levels are known to have adverse effects on the behaviour and physiology of laboratory animals, yet their acoustic environment is rarely monitored. In particular, high-frequency sounds that are above the limit of human hearing, but are well within the limits of many laboratory species (i.e., ultrasounds), are usually ignored. In this study, the acoustic environment of laboratory animals was investigated in a variety of different animal facilities. Sound pressure levels (dB SPL) were monitored for periods up to 24 h over two frequency ranges: a relatively low range (0.01-12.5 kHz), and a high range (12.5-70 kHz). While background sound levels in undisturbed situations were generally low (i.e., below 50 dB SPL), marked increases in sound levels often occurred during the working day, producing characteristic daily variations in the sound profile. Peak SPLs commonly reached values of 80-95 dB in the low-frequency range and 50-75 dB in the higher range. In most cases, sound levels were low over weekends. The results suggested that human activities were a very important source of sound in most animal facilities. In a few situations (e.g., rabbits, marmosets, dogs), the animals themselves provided a significant contribution to the acoustic environment. It is clear that the acoustic environment of laboratory animals is a daily variable that is usually uncontrolled and that may have important implications for behavioural and physiological experiments and for animal welfare.

Descriptors: animal welfare, arousal, noise, social environment, Callithrix, cats, circadian rhythm, ferrets, loudness perception, mice, pitch perception, psychoacoustics, rabbits, rats, sound spectrography, species specificity, ultrasonics.

Mizisin, A.P., M.W. Kalichman, R.S. Garrett, and K.C. Dines (1998). **Tactile hyperesthesia, altered epidermal innervation and plantar nerve injury in the hindfeet of rats housed on wire grates.** *Brain Research* 788(1-2): 13-19.

AB-The effects of wire grates on nerve injury and recovery were examined in rats housed in cages with sawdust-covered solid flooring. For the first 3 weeks of the study, 20 rats were housed on sawdust alone and 20 rats were housed in cages with wire grates placed over the sawdust. For the remaining 9 weeks, 10 animals housed on sawdust had wire grates added to their cages, while grates were removed from the cages of 10 animals. The effects of tactile stimulation on hindpaw plantar skin was measured weekly using the Von Frey filament test. Intraepidermal innervation using PGP 9.5 immunostaining and plantar nerve histology were assessed at the end of the 12-week study. After just 1 week on grates, hindpaw withdrawal thresholds were already markedly decreased and remained low until the grates were removed at 3 weeks. Thresholds returned to normal by 4 weeks after removal of the grates. Wire grates also induced increases in PGP 9.5 immunoreactive intraepidermal fine nerve endings that were normalized after grate removal. Demyelination, Wallerian degeneration and Renaut bodies were induced in the medial plantar nerve in rats housed in cages with wire-grate flooring. Nerve injury was largely resolved



after 9 weeks on sawdust flooring. These data demonstrate that wire grates rapidly induce hindpaw tactile hyperesthesia and plantar neuropathy in rats and emphasize a risk of using wire-grate cage flooring in studies assessing hindlimb function and structure.

Descriptors: epidermis innervation, foot innervation, hyperesthesia, peripheral nerves injuries, hindlimb, housing, immunohistochemistry, Sprague-Dawley rats, wire-bottoms.

Olfert, E. D. (1998). **A rodent's-eye view of environmental enrichment: Asking the animal what it prefers.** *CALAS/ACSAL Newsletter* 32(5): 9-13.

NAL call number: SF405.5 C36

Descriptors: behavioral needs, natural behavior, preference testing, interpreting results, strength of a preference, preference and animal welfare, floor types, bedding, nesting material, shelters, enrichment devices, nest boxes, mice, rats, the "preferred mouse cage," the "preferred rat cage."

Perez, C., J.R.Canal, E. Dominguez, J.E. Campillo, M. Guillen, M.D. Torres (1997). **Individual housing influences certain biochemical parameters in the rat.** *Laboratory Animals* 31(4): 357-61, NAL call number: QL55 A1L3

AB-Individual housing has been reported to modify animal behaviour. The present study compares the plasma levels of glucose, triglycerides and total cholesterol, weight, and food and water intake in two groups of female rats. Group A: 10 rats who remained grouped in two cages for 21 days; and Group B: 10 rats housed in two cages for 7 days, then isolated in individual cages from day 8 to day 15, and finally grouped together again for the last 7 days of the study. The results showed that the plasma values of glucose declined ( $P < 0.05$ ) in the Group B rats when they had been returned to group condition ( $4.79 \pm 0.72$  mM) than when they had been isolated ( $5.45 \pm 0.94$  mM). Plasma triglyceride levels were lower ( $P < 0.05$ ) in isolated rats ( $0.70 \pm 0.26$  mM) than in any determination of the grouped rats. Group B: 1st week  $1.21 \pm 0.21$  mM, 3rd week  $0.88 \pm 0.20$  mM; and Group A:  $1.22 \pm 0.20$ ,  $0.96 \pm 0.16$ , and  $0.96 \pm 0.36$  mM, in the first, second, and third week, respectively. There were no statistically significant differences in total cholesterol values as a function of the individual housing of animals. While there was no weight difference between the two groups of rats that could be ascribed to individual housing, there was a statistically significant increase ( $P < 0.05$ ) in the food intake of isolated rats ( $17.5 \pm 3.2$  g) with respect to values in the same Group B animals when they were housed together (1st week,  $16.6 \pm 2.8$  g; 3rd week,  $16.8 \pm 3.1$  g). These results therefore confirm that individual housing of female rats provoke variations in certain biochemical parameters, and that if this is not taken into account in performing different scientific studies, it could give rise to unreliable or even dubious results.

Descriptors: animal behavior, animal physiology, pH, blood glucose analysis, cholesterol, housing, triglycerides, drinking, eating, Wistar rats, social isolation.

Perkins, S.E. (1996). **Evaluation of microenvironmental conditions and noise generation in three individually ventilated rodent caging systems and static isolator cages.** *Contemporary Topics in Laboratory Animal Science* 35(2): 61-65.

NAL call number: SF405.5 A23

Descriptors: caging, contaminants, environmental temperature, relative humidity, carbon dioxide, ammonia, noise level, significant differences reported between cage types for all parameters measured, mice.

Raynor, T.H., W.H. Steinhagen, and T.E. Hamm (1983). **Differences in the microenvironment of a polycarbonate caging system: bedding vs raised wire floors.** *Laboratory Animals* 17(2): 85-9.

NAL call number: QL55 A1L3

AB-The microenvironment of polycarbonate cages housing rats with and without various types of bedding was compared with that of cages that utilized wire floor inserts with different bedding types. Parameters monitored were temperature, humidity, ammonia concentrations and particulates. No differences were noted in the various caging types in relation to temperature and

humidity measurements. Significant differences in ammonia concentrations existed in some of the cages when bedding material was used. The use of raised floorwalk inserts also demonstrated significant differences in particulate counts to cages without inserts. The data obtained demonstrated that contact bedding was useful in controlling ammonia generation and that a raised floorwalk insert reduced significantly the aerosolization of bedding particles that could be ingested or inhaled by the rats.

Descriptors: animals, housing ammonia, animal husbandry, bedding, humidity, polymers, rats, temperature.

Rock, F.M., M.S. Landi, H.C. Hughes, R.C. Gagnon (1997). **Effects of caging type and group size on selected physiologic variables in rats.** *Contemporary Topics in Laboratory Animal Science* 36(2): 69-72.

NAL call number: SF405.5 A23

Descriptors: caging, group-size, body temperature, heart rate, blood pressure, feed intake, body weight, animal husbandry, rats, motor activity, cage types had significant effects on motor activity and feed intake.

Salvin, S.B., B.S. Rabin, and R. Neta (1990). **Evaluation of immunologic assays to determine the effects of differential housing on immune reactivity.** *Brain, Behavior, and Immunity* 4(3): 180-8.

AB-The mechanism is being investigated to determine specifically how an environmental variation such as differential housing can influence the multiple components of the host defense mechanism. Male C3H/HeJ mice were housed either one or five per cage. Cells and sera from these mice were analyzed and compared by several immunologic techniques to determine in which cells or tissues the effect of differential housing was most pronounced. The individually housed mice (a) had a greater capacity to phagocytose dead cells of *Candida albicans*. (b) had spleens that produced more macrophage colony stimulating factor (M-CSF). (c) were more responsive to M-CSF, (d) had peritoneal macrophages that released greater quantities of interleukin-1 in vitro into the surrounding medium and that had a greater capacity to migrate toward a chemotactic stimulus, and (e) had higher titers of IgM hemagglutination antibody to sheep erythrocytes. Differential housing of mice may therefore be a highly important modulator and indicator of the nature and extent of an animal's immunologic response to an environmental stimulus.

Descriptors: antibody formation, housing, cellular immunity, leukocyte chemotaxis, hemagglutination tests, hematopoietic stem cells, drug effects, IgM biosynthesis, interleukin-1 secretion, macrophage colony-stimulating factor--pharmacology, macrophages, mice, inbred C3H mice, peritoneal cavity, phagocytosis, spleen cytology, chemical stimulation.

Weerd, H. A. van de, P.L.P. van Loo, L.F.M. van Zutphen, J.M. Koolhaas, and V. Baumans (1998). **Strength of preference for nesting material as environmental enrichment for laboratory mice.** *Applied Animal Behaviour Science* 55(3/4): 369-382.

NAL call number: QL750 A6

Descriptors: environmental enrichment, nesting mice, cages, litter, floor husbandry; floor type, animal behavior, animal welfare, wire-bottoms.

Weerd, H.A. van de, F.A.R. van den Broek, and V. Baumans (1996). **Preference for different types of flooring in two rat strains.** *Applied Animal Behaviour Science* 46(3/4): 251-261.

NAL call number: QL750 A6

AB-Bedding material is a permanent part of the environment of laboratory rodents. In the present study, rats of two strains (Wistar HsdCpb:WU and Brown Norway BN/SsNCpbHsd) were placed in a preference test system to evaluate their preference for three types of bedding material (sawdust, softwood shavings and paper particles) compared to wire mesh. The rats showed a significant preference for the cages with wood shavings and paper bedding, both consisting of



large particles. The paper bedding may serve as an alternative to wire mesh floor in some (e.g. toxicological) studies, because of its defined composition. The cages with sawdust and wire mesh floor were relatively avoided. Rats slept in the cages with large-particle bedding, but used the other cages for active behaviour such as eating and defecating; furthermore, many rats preferred different cages during day and night. It is suggested that different behavioural activities may require different cage floor covering.

Yoganathan, S., T.A. Wilson, and R.J. Nicolosi (1998). **Housing conditions effect plasma lipid concentrations and early atherogenesis independent of treatment in hamsters.** *Nutrition Research* 18(1): 83-92.

NAL call number: 389.8 N954

Descriptors: lipoproteins, atherogenesis, atherosclerosis, housing, blood, hypercholesterolaemia, cholesterol, intake, triacylglycerols, hamsters, housing conditions affect plasma lipids.

Zochodne, D.W., M.N. Murray, P. van der Sloot, and R.J. Riopelle (1995). **Distal tibial mononeuropathy in diabetic and nondiabetic rats reared on wire cages: an experimental entrapment neuropathy.** *Brain Research* 698(1-2):130-136.

AB-Using electrophysiological recordings, we studied a distal tibial mononeuropathy that involves the hind foot of rats reared in cages with wire grid flooring. In an initial set of experiments, serial sciatic-tibial motor conduction recordings were made in smaller or larger rats reared in cages with wire grid or sawdust flooring. Electrophysiological features of the neuropathy were loss in the amplitude of the distal tibial nerve M potential recorded over hind limb foot muscles, temporal dispersion of the potential, often into multiple peaks, and a prolonged distal latency of the response. The changes in M amplitude were more apparent in larger rats with a greater body weight. In a second series of experiments we studied sciatic-tibial conduction over 16 weeks in nondiabetic rats and rats rendered diabetic with streptozotocin raised and wire grid or plastic flooring. Tibial mononeuropathy developed in both wire grid-reared groups, but there was evidence that it appeared earlier in diabetic rats.

Electrophysiological changes of distal mononeuropathy also obscured the expected slowing of sciatic-tibial motor conduction velocity from diabetics. Tibial mononeuropathy in rats reared on wire grid flooring may be a useful animal model of human entrapment neuropathy but its presence can confound studies of experimental neuropathy. Rats used in studies of experimental neuropathy should be housed in plastic cages with sawdust or shavings flooring.

Descriptors: experimental diabetes mellitus, diabetic neuropathies, housing, nerve compression syndromes, sciatic nerve, tibial nerve, analysis of variance, diabetes mellitus complications, Sprague-Dawley rats, wire-bottoms.

## Useful World Wide Web Sites

**Blood collection in mice using the saphenous vein - An alternative to retro orbital collection**  
[http://www.uib.no/vivariet/mou\\_blood/Blood\\_coll\\_mice\\_.html](http://www.uib.no/vivariet/mou_blood/Blood_coll_mice_.html)

The method has been developed by the Laboratory Animal Centre of the Norwegian Institute of Public Health by Annelise Hem and Per Solberg. Annelise Hem and Adrian Smith have submitted a paper on saphenous vein puncture to the journal "Laboratory Animals". They have successfully used this technique on mice, rats, hamsters, gerbils, guinea-pigs, mink and ferrets.

**Environmental Enhancement for Caged Rhesus Macaques-A Photographic Documentation**  
<http://www.primate.wisc.edu/pin/pef/slide/intro.html>

Defining improved 'psychological well-being' as having the option to actively express species-typical behavior patterns that were formerly inhibited due to a lack of appropriate stimuli, and experiencing less fear/distress in the presence of people, the author developed and implemented the following environmental enhancement plan for the center's colony of

approximately 700 caged rhesus macaques (*Macaca mulatta*).

**Guidelines for the Production of Polyclonal and Monoclonal Antibodies in Rodents and Rabbits**

<http://www2.ec.hscsyr.edu/dlar/antibody.htm>

This site is maintained by the State University of New York Health Science Center at Syracuse. The purpose of these Guidelines is to provide methods with demonstrated success that also minimize pain and distress for the laboratory animals employed in the technique.

**National Institutes of Health, Animal Research Advisory Committee (ARAC)**

<http://oacu.od.nih.gov/ARAC/toeclip.htm>

Recommendation on toe clipping of animals.

**University of Arizona Department of Animal Care**

<http://microvet.arizona.edu/Courses/MIC443/notes/handling.htm>

This site provides extensive information on handling, restraint, and techniques of laboratory rodents.

**University of Minnesota, Research Animal Resources**

<http://www.ahc.umn.edu/rar/housing.html#wirefloor>

Rodent cage floor policy.

**University of Minnesota, Research Animal Resources**

<http://www.ahc.umn.edu/rar/housing.html#Rodents>

Husbandry guidelines for laboratory animals.



# **Food Deprivation Or Water Deprivation**







# Guidelines for Diet Control in Behavioral Studies

Adopted by National Institutes of Health-Animal Care and Use Committee on 6/13/90.

Reapproved - 5/8/96.

Reapproved - 2/10/99.

This document is available at <http://oacu.od.nih.gov/ARAC/dietctrl.htm>

Behavioral research often requires that an animal perform a task for which it receives food or fluid reward. This situation is not unlike conditions in the wild, in which animals must forage, travel distances, solve problems, or otherwise work to obtain their food and water. In the professional judgement of many investigators, performing a task for rewards is behaviorally enriching for laboratory animals, especially nonhuman primates.

The purpose of this document is to provide investigators with guidelines for the proper use of diet control in behavioral studies.

## Food

Whenever an animal obtains any portion of its diet through food reward, the investigator must ensure that the sum of the nutritional value of the food earned through reward and of the food provided "free" (without the necessity of earning it) is sufficient to maintain the animal in a healthy state. Whenever possible, the food reward should be a "treat" (e.g., raisins, peanuts) which is sufficiently desirable and motivating for the animal that dietary restriction is unnecessary. However, dietary restriction may be justified in some cases, depending on the species, the behavioral task, and the requirements of the research proposal. In such cases, food must be provided every day, unless a specific exception to this policy has been obtained in an approved research proposal. In addition, weekly weight records must be kept, which should be available for examination by the veterinary staff and the ACUC.

If an animal under diet restriction loses more than 15% of its body weight (compared to its weight measured prior to the restriction) its food intake should be increased immediately until it regains its normal weight ( $\pm 15\%$ ). Exceptions to this policy will be allowed only if the attending or facility veterinarian determines that the weight loss does not endanger the health of the animal (as, for example, in the case of an animal that was initially overweight), or if prior approval has been obtained from the ACUC for the specific animal study proposal. Young, developing animals may have additional dietary requirements for maintaining their normal rate of growth; investigators working with young animals should specifically address this issue in their animal study proposal. The ACUC is aware that certain strains of large rats (e.g., Sprague-Dawley) may require up to a 20% loss of body weight before performing a behavioral task for rewards. Exceptions to the 15% maximum weight loss policy (up to a maximum of 20% weight loss) will be considered in such cases, but only if such strains are adequately justified in the animal study proposal.

## Fluid

As with food intake, whenever an animal obtains any portion of its fluid requirements through fluid rewards in behavioral testing, the investigator must ensure that the sum of the fluid earned through reward and the fluid provided "free" (without the necessity of earning it) is sufficient to maintain the animal in a healthy state. When water is not provided ad libitum, either the animal should be permitted to earn fluids to satiety during the period of behavioral training or its fluid intake should be appropriately supplemented on a daily basis.

In cases where supplements are required, the minimum amount of fluids to be provided daily should be equivalent to the amount typically consumed by the animal when either it is permitted to drink fluids to satiety or it is provided with water *ad libitum*. An exception to this policy will be made for the day immediately following a 24 hour or longer period in which the animal is provided with fluids *ad libitum*. On such days only, a reduced fluid supplement is permitted, but only if the normal supplement is demonstrated to interfere with behavioral training.

### **Assessment of adequacy of fluid intake**

Even though animals typically learn to meet all of their daily fluid requirement during the testing session, a number of precautions must be taken to avoid the possibility of acute dehydration or chronic fluid deficiency. The type (e.g. water, fruit juice) and concentration, if applicable, of the fluid reward should be specified in the animal study proposal. Daily records of fluid intake must be maintained and be available for review by the veterinary staff and the ACUC. Each animal under fluid restriction will be observed daily for health status by the animal care staff. If the Institute veterinarian determines that an animal is dehydrated on the basis of either physical examination or clinical pathological measurements, the animal's fluid intake must be immediately increased. A small but chronic fluid deficiency, however, may occasionally escape detection by physical observation.

Such chronic fluid deficiencies often result in a loss of body weight due to reduced food consumption. Therefore, as a further precaution against chronic deficiency, the animal's weight must be measured and recorded at no less than weekly intervals. If an animal shows a loss in body weight of more than 15%, fluids must be increased appropriately. Exceptions to this policy will be allowed only if the attending or facility veterinarian determines that an animal is adequately hydrated and that the weight loss does not endanger its health or prior approval has been obtained from the ACUC for the specific animal study proposal.

# Food or Water Deprivation Bibliography

Albee, R.R., J.L. Mattsson, B.L. Yano, and L.W. Chang (1987). **Neurobehavioral effects of dietary restriction in rats.** *Neurotoxicology and Teratology* 9: 203-211.

Descriptors: male Fischer rats, body weights, grip strength, body temperature, flash evoked potential, auditory brainstem response, somatosensory and cerebellar evoked responses, caudal nerve action potentials, cortical flicker fusion, feed restriction protocol involved feeding 15 percent (mild) or 50 percent (severe) less feed than controls had consumed (ad lib) the previous day, dietary restriction has significant effects on numerous behavioral and neurophysiological parameters that should be considered in the interpretation of data when body weight differences are present, diet restricted rats were more excitable while restrained for testing.

Driscoll, P., J.R. Martin, P. Kugler, and K. Baettig (1983). **Environmental and genetic effects on food-deprivation induced stomach lesions in male rats.** *Physiology and Behavior* 31(2): 225-228.

NAL call number: QP1 P4

AB-When Roman high- and low-avoidance (RHA/Verh and RLA/Verh) rats were individually housed in plastic cages with sawdust bedding and food-deprived (F-D) for 4-5 days, it was found that F-D RHA/Verh rats had more lesions than their unfasted controls and more lesions than F-D RLA/Verh rats. The lesions were mostly petechial in nature and located in the glandular portion of the stomach. Also, F-D RHA/Verh rats which were housed in the same room as the controls, as well as F-D RHA/Verh rats which were housed in a separate room with a strong food odor present, had more lesions than F-D RHA/Verh rats housed in the same separate room when there was no food odor, and when none of the rats present had access to food. When F-D RHA/Verh and F-D RLA/Verh rats were individually housed in metal cages with grid floors, however, a general increase in lesion scores resulted and differences between the two rat lines disappeared, as did differences among the room conditions. Also, many lesions were of an ulcerative nature and were located in the rumenal portion of the stomach. It was concluded that sensory (in this case olfactory, at least) and genetic factors are capable of playing roles in the induction of stomach lesions in rats, and that the type, extent and location of the lesions can depend upon whether or not the animals have access to sawdust bedding.

Descriptors: food deprivation, housing, odors, inbred rat strains, stomach ulcers, body temperature regulation, gastric acid secretion, purpura etiology, stomach diseases, wood, litter.

Hughes, J.E., H. Amyx, J.L. Howard, K.P. Nanry, and G.T. Pollard (1994). **Health effects of water restriction to motivate lever-pressing in rats.** *Laboratory Animal Science* 44(2): 135-140.

NAL call number: 410.9 P94

Descriptors: The objectives of this study were to determine the degree of water restriction necessary and sufficient to motivate acquisition and performance of a lever-press response in rats and the physiologic and general health effects of chronic daily restriction. Parameters examined included: hematological and clinical chemistry, body weight, gross necropsy, clinical examination.

Hohenegger, M., U. Laminger, P. Om, A. Sadjak, K. Guttman, and M. Vermes (1986). **Metabolic effects of water deprivation.** *Journal of Clinical Chemistry and Clinical Biochemistry* 24(5): 277-282.

NAL call number: RB40 A1Z4

Descriptors: dehydration, resuscitation, experimental disease.



- Horne, T., A. Gutman, S.H. Blondheim, and H.B. Aronson (1982). **Effects of 24 hour food and water deprivation on biochemical variables in blood.** *Israel Journal of Medical Sciences* 18(5): 591-595.  
 Descriptors: humans, 2.5 fold increase in plasma free fatty acids, 2 fold increase in bilirubin, significant increases in serum sodium, chloride, total proteins, albumin, uric acid, phosphorous, alkaline phosphatase, and aspartate aminotransferase, decrease in serum glucose and triglycerides, no changes in urea, potassium, cholesterol, or calcium.
- Kyriazakis, I. and C.J. Savory (1997). **Hunger and thirst.** In *Animal Welfare*, M.C. Appleby and B.O. Hughes, (eds.), Oxon, UK and New York: CAB International, pp. 49-62 .  
 NAL call number:  
 Descriptors: nutrient requirements, animal behavior, animal welfare, hunger, thirst, definitions, measurements of hunger, sources of malnutrition, sources of undernutrition, restriction, deprivation, welfare problems, behavioral problems related to restriction, stress related physiological problems, farm animals, laboratory animals.
- Laties , V. (1987). **Control of animal pain and distress in behavioral studies that use food deprivation or aversive stimuli.** *JAVMA (Journal of the American Veterinary Medical Association)* 191(10): 1290-1291.  
 NAL call number:  
 Descriptors: overview of food deprivation in behavioral studies, effects of feed restriction, effects of handling and injections, overview of studies where pain is being studies.
- Levin, S., D. Semler, , and Z. Ruben (1993). **Effects of two weeks of feed restriction on some common toxicologic parameters in Sprague-Dawley rats.** *Toxicologic Pathology* 21(1): 1-13.  
 AB-This study was intended to identify changes caused by short-term reduced feed intake in rats such as may occur with unpalatable feed or other forms of anorexia. For 2 wk, groups of rats (10/sex/group) were fed ad libitum (control group) or given 75% (mildly restricted group), 50% (moderately restricted group), or 25% (severely restricted group) of the amount of feed eaten the day before by controls. The control group and mildly restricted group grew steadily, but the terminal body weights of the mildly restricted group (both males and females) were only about 80% of controls. The moderately restricted group did not grow during the first week but grew slightly during the second week (terminal body weights about 65% of control). The severely restricted group lost weight throughout the study (terminal weight about 40% of control). Restricted groups exhibited hemoconcentration directly related to the degree of feed restriction. White blood cell counts were reduced (principally due to lymphopenia) in severely restricted rats. Platelet counts were decreased in all restricted groups. Total serum protein concentration was reduced (decreased globulins) in all female restricted groups and in the severely restricted males. The severely restricted rats had increased serum bilirubin, electrolyte derangements, and (in females only) decreased cholesterol. Thymus and liver weights (absolute and relative) were decreased in the moderately and severely restricted groups. All the feed-restricted groups had an increased incidence of superficial gastric erosions. The mildly and moderately restricted groups had slightly decreased hematopoietic tissue in sternal bone marrow, while the severely restricted group had bone marrow necrosis, thymic atrophy, and mild testicular degeneration. Findings in the severely restricted group were distinct from those in the other groups on the basis of their severity and were considered adverse. Changes in the mildly and moderately restricted groups were considered adaptive and innocuous since feed restriction of this degree has historically been associated with increased longevity and decreased disease incidence in chronic studies.

Levine, S. and A. Saltzman (1998). **An alternative to overnight withholding of food from rats.** *Contemporary Topics in Laboratory Animal Science* 37(3): 59-61.

NAL call number: SF405.5 A23

AB-Withholding of food overnight has been used for numerous experimental purposes, including to reduce errors of intraperitoneal injections by diminishing the size and weight of the gastrointestinal tract, to prepare for gavage or surgery, or to avoid the effects food in the gastrointestinal tract might exert on drugs or nutrients. However, withholding food overnight causes undesirable side effects including loss of body and hepatic weight and decreases in blood glucose concentrations. Withholding food from rats housed on bedding can also lead to ingestion of bedding. Providing rats with commercially available sucrose cubes overnight ameliorated these undesirable effects while still reducing the size of the gastrointestinal tract. Rats housed in cages without access to bedding had an additional reduction in weight of the gastrointestinal tract. Analysis of the results indicated that providing sucrose cubes overnight and reducing access to bedding was an effective alternative to overnight withholding of all food.

Descriptors: methods, food deprivation, fasting, digestive tract, drugs, body weight, hepatic weight, blood sugar, bedding, sucrose, liver, rats.

***Preparation and Maintenance of Higher Mammals During Neuroscience Experiments. Report of a National Institutes of Health Workshop, March 1991.*** Bethesda, Maryland: DHHS, Public Health Service, National Institutes of Health, 45 p.

NAL call number: HV4930 P74

Descriptors: prolonged non-survival recording procedures, survival anatomical procedures, perinatal procedures, food and water restriction, inducing neurological deficits, awake behaving preparations, animal care and use concerns, sample research protocols.

Ray, S. (1998). **An alternative to water deprivation techniques in animal learning studies.** *Animal Technology* 49(3): 113-120.

NAL call number: QL55 I5

AB- Many laboratories use a period of water deprivation to motivate animals on a variety of water reinforced learning paradigms including aversive conditioning and maze learning tasks. Such procedures can lead to long periods without water and increase inter-animal variability in learning performance. Reported is an alternative procedure using sucrose rich drinks, or sucrose solutions, as a reward in maze and discrimination learning procedures with no prior water deprivation. An initial experiment compares performance over trials of a water deprived group of rats learning to negotiate a Y maze, and a group of genetically matched animals running an identical maze with no water deprivation. Both groups negotiating the maze for a sucrose reward. Results show that non-deprived animals showed teaming that was equally as good as the water deprived animals. Similar results were confirmed in a Lashley jump stand discrimination task. The ability to study learning in non-deprived animals may be of great interest in studies of learned behaviour after lesion or other surgical interventions, when periods of dehydration may affect the animal's health. Further, the development of non-deprivation motivated techniques will reduce the severity of many commonly employed rodent learning paradigms. These results may also offer a useful heuristic to explore learning paradigms without food or water deprivation schedules in other species.

Schwartz, E., J.A. Tornaben, and G.C. Boxhill (1973). **The effects of food restriction on hematology, clinical chemistry, and pathology in the albino rat.** *Toxicology and Applied Pharmacology* 25(4): 515-524.

NAL call number:

Descriptors: body weight, blood enzyme levels, erythrocyte counts, hematocrit, alanine aminotransferase, alkaline phosphatase, blood glucose, platelets, blood urea nitrogen, leukocyte count, organ weight, sex factors, time factors.

Shimamura, T. and S. Trojanowski (1976). **Effects of repeated deprivation of drinking water on the structure of the renal medulla of rats.** *American Journal of Pathology* 84(1): 87-92.

NAL call number:

Descriptors: pathological changes in renal medulla, tubulointerstitial nephritis, dehydration.

Vermeulen, J.K., A. de Vries, F. Schlingmann, and R. Remie (1997). **Food deprivation: Common sense or nonsense?** *Animal Technology* 48(2): 45-54.

NAL call number: QL55 I5

AB-Overnight fasting (food deprivation) is a very common procedure in pharmacological research. One of the many reasons is to empty the animal's stomach. Solvay Duphar investigated the effects of overnight fasting and the possibility to shorten the period of the overnight fasting on male Wistar rats. In case of the effects being far-reaching (quality research and animal well-being), it might be necessary to develop an alternative method. This experiment fits very well in the concept of the 3 Rs of Russell and Burch. The experiment used 24 male rats. There were four experimental units. The rats were deprived respectively for 0 hours (controls), 6, 12, or 18 hours. This was done during the dark phase of the (facility) light cycle. A balance plateau was used for registration of animal behavior. After the deprivation, the animals were anesthetized with halothane (N<sub>2</sub>O/O<sub>2</sub>) and killed by decapitation. Liver weight, stomach contents, and bowel contents were parameters to be measured. Food deprivation causes severe changes in physiology and behavior of the rat. After six hours of food deprivation, the rat already has an empty stomach. The use of fasted rats in experiments seems only to be permitted when the duration of food deprivation is as short as possible.

Descriptors: experimental methods, animal behavior, drinking, eating, locomotion, grooming, resting, physiological changes.

## Useful World Wide Web Sites

### University of California at Irvine

<http://www.rgs.uci.edu/rig/asfluid.htm>

Policy for Food or Fluid Restriction

### University of Colorado Health Sciences Center, Animal Care & Use Program

<http://www.uchsc.edu/sm/animal/index.html>

Water and/or Food Restriction; To get to this policy, click on Animal Care Policies located under Training / Procedure Guides in the left frame on the web page.

### University of Vermont, Institutional Animal Care and Use Committee

<http://osp.uvm.edu/irbppm4f.htm>

Food or Fluid Restriction, Definitions, Policies and Guidelines



# **Pain Management and Humane Endpoints**







# Defining an Acceptable Endpoint in Invasive Experiments

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## Abstract

Animal Care Committees reviewing research protocols often demand an earlier endpoint to an experiment, for humane reasons. Scientists support the efforts to reduce potential pain and suffering, but may be reluctant to adopt earlier endpoints unless these can be objectively determined and will not invalidate the experimental data being collected. In this presentation a framework for objectively setting endpoints that may be scientifically supported will be presented. Crucial to this exercise is the involvement of all persons directly working with the animals, and their ability to observe the animals and make accurate assessments of their condition.

## Introduction

We have an obligation to minimize the potential pain and suffering experienced by an animal in the course of biomedical research. That sentiment is explicitly stated in ethical position statements of a number of organisations concerned with experimental animal use. For example, the Canadian Council on Animal Care (CCAC) *Ethics of Animal Investigation* (5) document says:

**"Animals must not be subjected to unnecessary pain or distress. The experimental design must offer them every practicable safeguard, whether in research, in teaching, or in testing procedures; ...**

Further, with respect to humane endpoints, the CCAC document says:

**"An animal observed to be experiencing severe, unrelievable pain or discomfort should be immediately killed, using a method providing initial rapid unconsciousness."; and, "Studies such as toxicological and biological testing, cancer research and infectious disease investigation may, in the past, have required continuation until the death of the animal. However, in the face of distinct signs that such processes are causing irreversible pain or distress, alternative endpoints should be sought to satisfy both the requirements of the study and the needs of the animal."**

One of the general ethical statements that has long been cited as guiding us to a more humane use of animals in research is the now famous 3R's tenet of Russell and Burch (15)--**Replacement** (of animals with other, non-sentient material), **Reduction** (of numbers of animals used), and **Refinement** (of technique "to reduce to an absolute minimum the amount of distress imposed on those animals that are still used."). Their book--*The Principles of Humane Experimental Technique* (15)--was a landmark publication, and still deserves to be consulted for its comments on the humane use of animals.

Although our ethical responsibilities seem quite clearly stated, these pronouncements do not answer the very important questions:

- How do we choose the endpoint that satisfies these principles?
- Where do we draw the line?
- How do we "refine" our experiments through establishing earlier, more humane endpoints to invasive animal experiments, particularly those that may have death as an endpoint?

This presentation will attempt to draw a framework for selecting an endpoint that reduces the potential for animal pain and suffering, and that hopefully will satisfy the experimental design requirements for objective evaluation.

### **Types of Studies Where Death of the Animal May be the Endpoint**

There are several types of studies where the death of the animal may be the endpoint as part of the experimental design. These would include; regulatory toxicology, diagnostic toxicology, acute toxicity studies in research; infectious disease studies, microorganism virulence challenge studies, vaccine efficacy trials; cancer research, cancer treatment evaluation, etc.

In some research investigations pain and suffering may unavoidably be part of the disease or condition being studied (e.g., some models of human diseases such as arthritis or cancer, and studies on pain, etc.).

Also, in some experimental animal uses, any pain and suffering is an unwelcome accompaniment to the animal use (e.g., monoclonal antibody production, Freund's Adjuvant use in antibody production, etc.). In these latter cases humane endpoints are relatively easy to define (e.g., limiting the volume and number of times a mouse with ascites is collected), and guidelines pertaining to these procedures already exist (6).

In all of these research endeavors, our responsibilities include the prevention and minimization of any unnecessary pain and distress for the animals. As the CCAC noted in *Ethics of Animal Investigation*, in the past the death of the animal may have been the endpoint in some experiments. Although quite conservative in tone, this CCAC statement acknowledges that pain and suffering may occur well before the animal is moribund.

In fact, the animal in a moribund state may be past suffering (and actually comatose). The observations that suggest an animal is "moribund" are quite clear. Before the animal gets to the point of being "moribund", however, our best judgements, based on the accuracy of our observations of the animal, will help set the earlier endpoint and thereby reduce the potential pain and suffering the animal is experiencing. Thus it is incumbent on us to continually refine our skills at seeking earlier endpoints for such experiments.

### **A Framework for Selecting an Earlier Endpoint**

There are several considerations in arriving at the objective assessment of pain and suffering, and translating that into the appropriate endpoint in a given experiment. Firstly, we must improve our skills at observing the animals and assigning some objective values to the observations we make (of animal behavior and physiology). Secondly, we need to know, in any given study, which observations are the most significant indicators of animal pain and suffering. Thirdly, we must have scientific acceptance of these measurements.

## Objectively Assessing Signs and Symptoms

With respect to the first point, the work of Morton and Griffiths in 1985 can be considered a landmark publication. They presented a set of criteria for assessing pain, distress, and discomfort in laboratory animals based on evaluating five aspects of an animal's condition. Those five aspects are: a) changes in body weight (including levels of food and water intake); b) external appearance; c) measurable clinical signs (e.g., changes in heart rate, in respiratory rate and nature); d) unprovoked behaviour; and e) behavioural responses to external stimuli. In each of these categories, a rating of 0 (normal or mild) to 3 (severe changes from normal) is made, the cumulative rating indicating increasing deviation from the normal in the animal. The cumulative rating is interpreted as an indication of increasing pain, distress, and suffering. **Table 1** presents this proposed scoring system in a checklist format.

**Table 1. Quantifying Pain / Distress / Suffering**

Variable	Score
<b>Body Weight Changes</b> 0 Normal 1 <10 percent weight loss 2 10-15 percent weight loss 3 >20 percent weight loss	
<b>Physical Appearance</b> 0 Normal 1 Lack of grooming 2 Rough coat, nasal/ocular discharge 3 Very rough coat, abnormal posture, enlarged pupils	
<b>Measurable Clinical Signs</b> 0 Normal 1 Small changes of potential significance 2 Temperature change of 1-2°C, cardiac and respiratory rates increased up to 30 percent 3 Temperature change of >2°C, cardiac and respiratory rates increased up to 50 percent, or markedly reduced	
<b>Unprovoked Behavior</b> 0 Normal 1 Minor changes 2 Abnormal, reduced mobility, decreased alertness, inactive 3 Unsolicited vocalizations, self mutilation, either very restless or immobile	
<b>Behavioral Responses to External Stimuli</b> 0 Normal 1 Minor depression/exaggeration of response 2 Moderately abnormal responses 3 Violent reactions, or comatose	
<b>TOTAL SCORE</b>	

Adapted from: Morton, D.B. and P.H.M. Griffiths (1985). *Veterinary Record* 116: 431-436.

The British Association of Veterinary Teachers and Research Workers (AVTRW) (16) has developed a set of guidelines for the recognition and assessment of pain in animals to assist scientists in their compliance with the British Animals (Scientific Procedures) Act of 1985. Specific



information on the behavioral and physiological changes in the various animal species that may indicate the presence of pain are published (16, 19). The report of a committee of the British Laboratory Animal Science Association (19) includes an assessment of the severity of a wide variety of procedures performed on animals in the course of biomedical research. A number of other publications are also available to help identify the signs and symptoms of experimental animal pain, distress, and suffering (1, 2, 3, 4, 9, 18).

The publications of Morton and Griffiths (13) and the British Association of Veterinary Teachers and Research Workers (16) focus on an important matter--that of trying to make more objective assessments of the pain, distress, and suffering that may occur in an animal in the course of biomedical research.

In addition to general signs of pain and distress, there are the specific signs and symptoms related to the condition being studied. For most animal models of disease, information on the organ system(s) affected, the specific symptoms, the progression of symptoms, the time course of the disease condition, and the expected lesions, is available from the general veterinary and laboratory animal science literature. Such specific signs and symptoms must also be used in the overall evaluation of the animal's condition, on which selection of the endpoint will be based.

### **Identifying Significant Indicators of Pain and Suffering**

The next problem is deciding, in any given animal model, which of the many possible observations and measurements are the most important or significant indicators of the condition of the animal, or perhaps more importantly from the scientist's perspective, which are indicators of an irreversible deteriorating condition of the animal. This is not an easy task, since a large number of different behavioral observations and physiological measurements are possible. Two papers dealing with the adjuvant-induced arthritis model in the rat provide insight into the difficulties in finding / choosing the right observations (4, 9).

To determine which behaviors in arthritic rats correlated with progression of the induced arthritis, Butler et al. (4) conducted detailed behavioral studies. This was done by measuring the frequency of a wide range of specific behaviors with the use of videotape computer analysis. The time arthritic rats spent performing 12 specific behaviours was measured; rearing, sniffing, food-hoarding, grooming, scratching, freezing (arresting), resting, sleeping, running, climbing, eating and drinking. Although changes in the frequency of several behavior patterns were found (decreased rearing, running, eating, drinking and climbing; increased resting, freezing, scratching), the conclusion was that of all these changes in behavior, increased scratching was the most significant behavioral change that tied in with developing arthritis, indicating chronic pain.

Such behavioral evaluations (4, 9) are research projects in themselves, involving many hours of technical time, with expensive monitoring and analytical equipment. It may be unrealistic to demand a similar degree of preliminary behavioral evaluation each time an animal-based research program is begun where the potential for pain and distress are high (mice in a liver cancer research program, for example). Nevertheless, conducting a pilot study to establish the observational criteria to be used to set the endpoint may be a very useful exercise, particularly at the onset of a research program that may be ongoing.

### **Scoring of Significant Behavioral and Physiological Observations to Set Endpoints**

As noted above, information on the general signs of pain, distress and suffering for the various animal species commonly used in biomedical research are readily available (1, 2, 3, 4, 9, 16, 18). Of these, significant weight loss may be one of the more important signs of deterioration in the animal's condition (reflecting a change in food and water consumption).

For some specific areas of biomedical research, particularly in cancer research, more detailed criteria for selecting the endpoint have been proposed by Montgomery (11, 12), Redgate, Deutsch and Boggs (14), and the United Kingdom Coordinating Committee on Cancer Research (UKCCCR) (20).

Table 2 presents some specific clinical abnormalities that are useful indicators in cancer research and toxicologic studies (11, 12). Table 3 presents some of the endpoint criteria, physiological, behavioral and pathological, that Montgomery (12) identified for euthanasia of moribund animals.

One of the scientific concerns about arbitrarily establishing an early endpoint, particularly in cancer therapy studies, is that early euthanasia may alter longevity or survival data which are an important indicator of "successful" treatment. For example, the "successful" treatment of cancer in a group of rats which resulted in them living a month longer, might be masked by early euthanasia based only on clinical observations. In such cases, finding the signs of disease and distress that point to an irreversible deterioration in the animal is important. Redgate, Deutsch and Boggs (14), in their examination of a brain tumor model in a rat (9L gliosarcoma in Fischer 344 rats), concluded that a weight loss period of more than 6 days had a high correlation with irreversible progression to death, regardless of which treatment group was studied. In this model then, an endpoint that satisfied the scientific concerns could be established at the end of a 6 day period of consecutive weight loss (which in this case was about 10 days before death of the animals).

The UKCCCR Guidelines for the welfare of animals in experimental neoplasia (20) contain some general recommendations for endpoints; when tumor size exceeds 10 percent of body weight, or if weight loss exceeds **20 percent** (these would be in the maximum score category in the Morton and Griffiths proposal, indicating severe negative effect on the animal).

**Table 2. Selected Clinical Observations Used in Cancer Research and Toxicological Studies**

Parameter	What to Look for
General Appearance	Dehydration, decreased body weight, missing anatomy, abnormal posture, hypothermia, fractured appendage, swelling, tissue masses, prolapse, paraphimosis
Skin and fur	Discoloration, urine stain, pallor, redness, cyanosis, icterus, wound, sore, abscess, ulcer, alopecia, ruffled fur
Eyes	Exophthalmos, microphthalmia, ptosis, reddened eye, lacrimation, discharge, opacity
Nose, mouth, and head	Head tilted, nasal discharge, malocclusion, salivation
Respiration	Sneezing, dyspnea, tachypnea, rales
Urine	Discoloration, blood in urine, polyuria, anuria
Feces	Discoloration, blood in feces, softness/diarrhea
Locomotor	Hyperactivity, hypoactivity, coma, ataxia, circling, muscle, tremors, convulsion/seizure, limb paralysis, prostration

Montgomery, C.A. Jr. (1990). *Cancer Bulletin* 42(4): 230-237.

Siems and Allen (17) recommended that the endpoint in a disease model (chronic infection with systemic *Candida albicans*) be set at (among other measurements) the point when the animals lose more than 20 percent of body weight, or when the body temperature drops more than 4°C (both of which are easily monitored). The magnitude of these changes from normal would also give a maximum score on the Morton and Griffiths proposal, indicating severe negative effects on the animal.

Thus, there is a good body of information developing on selecting more humane endpoints based on clinical observations of the animals in a variety of biomedical research areas. The development and use of observational checklists for scoring the animal's condition in a study provides for an objective basis on which decisions about endpoints can be made. The advantages of checklists are the same here as for airline pilots; nothing is overlooked or taken for granted. The other real advantage is that such checklists help us to improve our observational capabilities, particularly with the smaller laboratory animals where some of the conventional clinical observations made on larger animals are not so useful (e.g., temperature, heart rate, respiratory rate).

Another matter that must be addressed is the frequency with which the observations should be made. It is generally accepted that normal healthy animals should be observed at least once a day (8). However, once an animal is in a potentially critical period with respect to impairment, more frequent observations must be demanded. But what is adequate? Montgomery (12) suggests that at least two observations daily should be made; more often during critical times. The sensitivity and judgement of the animal care committee review process will help determine what is acceptable.

**Table 3. Selected Criteria For Euthanasia of Moribund Animals**

Rapid weight loss (15-20 percent within a few days)
Extended period of weight loss (progressing to emaciated state)
Spreading area of alopecia caused by disease
Rough hair coat, hunched posture, distended abdomen, or lethargy, especially if debilitating or prolonged (3 days)
Diarrhea, especially if debilitating or prolonged (3 days)
Coughing, rales, wheezing, and nasal discharge
Distinct icterus and/or anemia
Rapid growth of mass or masses, or clinical signs of neoplasia
Central nervous system signs such as head tilt, tremors, spasticity, seizures, circling, or paralysis or paresis, especially if associated with anorexia
Frank bleeding from any orifice
Markedly discolored urine, polyuria, or anuria
Persistent self-induced trauma
Lesions interfering with eating or drinking
Clinical signs of suspected infectious disease requiring necropsy for diagnosis
Other clinical signs judged by experienced technical staff to be indicative of moribund condition

Montgomery C.A. Jr. (1990). *Cancer Bulletin* 42(4): 230-237.



## The Role of the Institution's Animal Care Committee

The role of the animal care committee is vital in establishing the structure that will ensure earlier endpoints are used. With respect to setting and determining humane endpoints, each individual's responsibilities should be clearly defined, and a clear chain of consultation established. This is particularly important for dealing with unanticipated negative effects on the animals in an invasive study.

Some of the questions that might help a protocol review committee ensure that an acceptable, humane endpoint will be in place include:

- What are the scientific justifications for using death or "moribund" as the proposed endpoint?
- What is the expected time course for the animals, from initial treatment to first signs of pain/distress to the death of the animal, based on previous information with the specific model under study?
- When are the effects to the animal expected to be the most severe?
- Has a "checklist of observations," on which the endpoint will be based, been established?
- If the course of the disease and expected signs of the negative effects are unknown, could an initial (pilot) study, under close observation by the laboratory animal veterinary staff, answer these questions?
- Who will monitor the animals (identify all responsible)?
- What will be the frequency of animal observations: a) during the course of the study, and b) during critical times for the animals?
- Do the animal care and technical staff have the training and expertise to monitor the animals adequately?
- What provisions have been made to deal with any animals that show unexpectedly severe signs and symptoms?

## Summary

All of us involved in biomedical research, from the scientist and the animal care staff, to the laboratory animal veterinarians and the animal care committees, have responsibilities for the humane care and use of experimental animals. In establishing humane endpoints, the institutional animal care committee should ensure that acceptable criteria are used by the principal investigator to determine the endpoint. Through the use of observational checklists and animal condition scoring systems, objective, humane endpoints can be identified. Responsibilities for observing and monitoring the animal's condition must be clearly delineated. Persons involved in establishing and effecting humane endpoints in invasive experiments are encouraged to present and publish this data, to support our efforts at continually refining the animal use practices that occur in biomedical research.



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# Endpoints in Animal Study Proposals

Guideline Approved by the National Institutes of Health Animal Research Advisory Committee on October 9, 1996 and reapproved February 10, 1999. It is available at <http://oacu.od.nih.gov/ARAC/endpoint.htm>

## Morbidity

Every effort should be made to minimize pain and distress experienced by animals used in research. However, experimental studies may involve procedures that cause clinical symptoms or morbidity in animals. Optimally, studies are terminated when animals begin to exhibit clinical signs of disease if this endpoint is compatible with meeting the research objectives. Such endpoints are preferable to death or moribundity as endpoints since they minimize pain and distress.

Animal Study Proposals involving morbidity as an endpoint should address the following:

1. Criteria that establish when the endpoint has been reached. There are several examples in the literature that might be considered, including:

- Evaluation of five aspects of an animal's condition as described by Morton and Griffiths. These are body weight, physical appearance, measurable clinical signs, unprovoked behavior and response to external stimuli.
- Clinical observations used in cancer research and toxicological studies as described by Montgomery. Parameters include changes in general appearance, skin and hair, eyes, nose, mouth and head, respiration, urine, feces and locomotion.
- General clinical signs that constitute an endpoint include, but are not limited to:
  1. Rapid weight loss.
  2. Diarrhea, if debilitating.
  3. Spreading alopecia caused by disease.
  4. Rough hair coat, hunched posture, lethargy or persistent recumbency.
  5. Coughing, labored breathing, nasal discharge.
  6. Jaundice and/or anemia.
  7. Neurological signs.
  8. Bleeding from any orifice.
  9. Self-induced trauma.
  10. Any condition interfering with eating or drinking.
- Additional signs in neoplasia studies that constitute an endpoint include, but are not limited to:
  1. A tumor burden greater than 10% bw, and in an adult mouse, a mean tumor diameter not exceeding 20 mm or in an adult rat, a mean tumor diameter not exceeding 40 mm. Formulas for calculating tumor size can be found in the literature (see ref.).
  2. Tumors that ulcerate, become necrotic or infected.
- Any animal found unexpectedly to be moribund, cachectic, or unable to obtain food or water.

2. A plan for monitoring the animals both before and after a change in any of the above aspects, providing care if appropriate, and increasing monitoring from once a day to twice or more a day.

Monitoring or clinical care on weekends and holidays may require involvement of the investigative staff to supplement that provided by the animal care staff.

3. Identification of personnel responsible for evaluation, record keeping, notification of the investigator and/or veterinarian and persons responsible for euthanasia.

## Endpoint references:

Morton and Griffiths (1985), *Veterinary Record* 116:431-43.  
Montgomery (1990), *Cancer Bulletin* 42:230-237.

## Tumor size references:

Bullard et al. (1981), *J. Neuropath. Exp. Neurol.* 40:410-427.  
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Welch et al. (1994), *Oncogene* 9: 255-262.

## Death or Moribundity

Death or moribundity as an endpoint may be necessary for some research projects. The moribund condition is defined as a clinically irreversible condition leading inevitably to death. In these studies, animals are permitted to die or become moribund, as a result of experimental procedures. In some cases, pain relieving measures are not used because such measures may compromise the experimental integrity of the study. Examples of research proposals that may have death or moribundity as an endpoint include: infectious disease studies, drug and toxicity studies, and cancer research. The following guidelines are suggested to assist the ICD Animal Care and Use Committees in reviewing proposals with death or moribundity as endpoints.

Animal Study Proposals utilizing death or moribundity as an endpoint should contain the following information:

1. The scientific rationale for death or moribundity as an endpoint, including:
  - a. What alternatives were considered, why morbidity as an endpoint cannot be used, and how alternatives will be used whenever possible.
  - b. Why pain relieving measures cannot be utilized.
  - c. Number of animals to be used and why this is the minimal number of animals required.
  - d. Whether animals will be euthanized when moribund and if not, what information is to be gained in the interval between moribundity and death.
2. Acknowledgment of the following animal care and monitoring procedures:
  - a. Animals involved in experiments that may lead to moribundity or death will be monitored daily by personnel experienced in recognizing signs of morbidity (illness, injury, or abnormal behavior) for at least the following:
    1. Abnormal appearance: abnormal posture, rough hair coat, head tucked into abdomen, exudate around eyes and/ or nose, skin lesions, or abnormal breathing.
    2. Abnormal activity: difficulty with ambulation, decreased food or water intake, or self mutilation.
  - b. The frequency of observation will be increased to at least twice daily when animals exhibit the above or other signs of moribundity. Monitoring on weekends and holidays may require involvement of the investigative staff to supplement that provided by the animal care staff. Designated personnel, including the attending veterinarian, should be notified as soon as animals



show signs of disease. An assessment of the animals condition should be made as soon as possible and a plan of action established.

c. Consideration will be given to moving animals to individual cages when their condition deteriorates to the point that injury from other animals or cannibalism is likely. Dead animals must be promptly removed.

d. Written records will be kept of all monitoring.

Hamm (1995), Contemporary Topics 34:69-71.

# Assessment and Alleviation of Post-Operative Pain

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Abstracted by Paul Flecknell from his book *Laboratory Animal Anaesthesia* 2nd Edition, 1996, and presented at the CALAS/ACTAL Convention in Prince Edward Isle, Canada

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The effective alleviation of post-operative pain in laboratory animals should be considered an important goal in all research establishments. Despite the emphasis given to humane treatment of laboratory animals in the national legislation of many countries, analgesia may still not be administered routinely in the post-operative period. This omission is particularly common when the animals concerned are small rodents. When analgesics are administered, assessment of methods of pain recognition or severity may account in part for the relatively infrequent use of analgesics in animals, in comparison to their use in man. This is not meant to imply that veterinary surgeons and others involved in animal care are incapable of recognizing that an animal is in pain, but preconceptions about animal pain may limit the value of any assessment of its severity (see below).

Although we would wish to alleviate pain because of concerns for animal welfare, a number of counterarguments have been advanced to justify withholding analgesics:

*Alleviation of post-operative pain will result in the animal injuring itself.* Provided that surgery has been carried out competently, administration of analgesics, which allow resumption of normal activity, rarely results in problems associated with the removal of pain's protective function. Claims that analgesic administration results in skin suture removal are unsubstantiated, and contrary to findings in our laboratory. In certain circumstances, for example after major orthopaedic surgery, additional measures to protect and support the operative site may be required, but this is preferable to allowing the animal to experience unrelieved pain. All that is required in these circumstances is to temporarily reduce the animal's cage or pen size, or to provide additional external fixation or support for the wound. It must be emphasized that these measures are very rarely necessary, and in our institute, administration of analgesics to laboratory animals after a wide variety of surgical procedures has not resulted in any adverse clinical effects.

*Analgesic drugs have undesirable side-effects such as respiratory depression.* The side-effects of opiates in animals are generally less marked than in humans and should rarely be a significant consideration when planning a post-operative care regimen.

*We don't know the appropriate dose rates and dosage regimens.* This is primarily a problem of poor dissemination of existing information. Virtually every available analgesic drug has undergone extensive testing in animals. Dose rates are therefore available for a range of drugs in many common laboratory species (17, 36). It is occasionally difficult to extrapolate available dose rates from one species to another and to translate dose rates that are effective in experimental analgesiometry into

dose rates which are appropriate for clinical use. Nevertheless, in most instances, a reasonable guide as to a suitable and safe dose rate can be obtained.

*Pain relieving drugs might adversely affect the results of an experiment.* Although there will be occasions when the use of one or another type of analgesic is contra-indicated, it is extremely unlikely that there will be no suitable analgesic that could be administered. More usually, the reluctance to administer analgesics is based upon the misconceived idea that the use of any additional medication in an experimental animal is undesirable. The influence of analgesic administration in a research protocol should be considered in the context of the overall response of the animal to anaesthesia and surgery. The responses to surgical stress may overshadow any possible adverse interactions associated with analgesic administration. An additional consideration is that many arrangements for intraoperative care fail to control variables such as body temperature, respiratory function and blood pressure. It seems illogical to assume that changes in the function of the cardiovascular or respiratory systems are unimportant, but that administration of an analgesic will be of overriding significance. It should be considered an ethical responsibility of a research worker to provide a reasoned, scientific justification if analgesic drugs are to be withheld. It is also important to realize that the presence of pain can produce a range of undesirable physiological changes, which may radically alter the rate of recovery from surgical procedures (28).

## PROGRESS IN PAIN ASSESSMENT

When debating the nature of pain in animals, considerable parallels can be drawn with the situation in human infants. In adult humans, the ability to provide direct verbal communication, complete pain questionnaires or scoring systems, or to directly manage analgesic dosage using patient controlled analgesia systems allows reasonably reliable estimates to be made of the degree of pain and the efficacy of pain control. In young human infants, written and verbal communication is not possible, nevertheless, extrapolation from adult humans, coupled with objective demonstrations of the adverse effects of surgical stress, has led to a huge increase in interest in providing pain relief to these patients (2, 41).

The approaches used in human infants can provide a framework for animal pain assessment. The most widely used techniques have been pain scoring systems based upon criteria such as crying, facial expression, posture and behaviour (42). This type of approach was advocated as a means of assessing pain and distress in animals (43). This paper influenced a large number of other groups, who modified the original hypothesis, but retained the central notion of identifying pain specific behaviours, and rating them in some way (3, 18, 33). Surprisingly, progress in validating this hypothesis has been remarkably slow. An early report (35) indicated that the technique could be applied successfully, but the few subsequent published data are less encouraging. Particular problems noted were considerable between observer variation and the poor predictive value of certain of the parameters scored (5, 6). The between observer variation is not unexpected, and parallels problems recognized in human pain scoring. It appears that if the number of observers is restricted, and the criteria used carefully selected, reasonable agreement can be achieved (49).

The basic methodology—selecting clinical signs which might be due to pain—has been used to provide pain-scoring systems in veterinary clinical patients. Attempts at scoring have either used descriptive ratings converted to numerical scores to allow statistical analysis, or have used visual analogue scoring systems (VAS) (45, 46, 48, 49, 53). A problem with many of these studies is the difficulty associated with scoring of animal behaviour in a relatively brief period. If it is believed that behavioural responses can indicate pain, and hence the efficacy of analgesia, then more detailed assessments are likely to be required. Support for the value of behavioural observations is provided by studies of the effects of tail docking and castration in lambs (54) and castration in piglets (40).



In laboratory animals, a number of different approaches have been used to assess pain or distress. The most extensive studies have been undertaken to investigate chronic pain, for example, those by Colpaert et al (8, 9, 10, 11), using an adjuvant arthritis model in the rat. Body weight, minute volume of respiration, mobility, vocalizations, specific behaviours and self-administration of analgesics were all considered as indices of pain. When discussing the results of these investigations, the authors concluded that all of the parameters responded to the same stimulus, and that the most reasonable explanation was that they were influenced by the presence of pain (9). Motor behaviour changes have been suggested as indices of pain (7, 55) and loss of appetite and reduction in body weight have been noted in rodents post-operatively (23, 24, 55). Recently, these variables have been studied in rats as potential means of assessing the degree of post-operative pain, and comparing the efficacy of different analgesic regimens (20, 21, 37, 38). As with other pain assessment techniques in animals, these assumed that if a change to a variable occurred after a procedure that would cause pain in man, then the change may be related to pain in the animal. If administration of an analgesic reverses the changes associated with the procedure, this supports the hypothesis that the changes were, at least in part, pain related. Clearly it is important to establish that the analgesic did not have non-specific effects in normal animals that would influence the variable studied. This is a somewhat circular argument, since it is simply stating that indices of pain are those indices that are normalized by administration of analgesic drugs. Although efficacy of these analgesics in reducing peripheral input in animals is well-established, (1, 13, 31, 52), their effects on clinical pain are only validated in humans.

The uncertainty surrounding pain scoring could be circumvented if some independent validation method were available. In man, a series of objective criteria have been proposed to assess pain. These have included pulse rate, skin conductance and resistance, blood pressure and skin temperature. In addition, biochemical and endocrine parameters, such as blood corticosterone or cortisone concentrations or catecholamine concentrations, have been proposed as indicating pain. A major problem in interpreting the significance of these changes is the influence of surgery and anaesthesia, which markedly alter many of these variables, even in patients which are pain free (29). The surgical stress response occurs in all patients, and although it can be reduced by intra-operative use of opioids, it occurs even in patients who receive a high level of post-operative pain control. In man, catecholamine and cortisol responses have shown to be poorly correlated with post-operative pain scores. Use of these variables in animals has the same constraints. Catecholamine rises have been demonstrated in cats (4) and dogs (48), and cortisol response is less following thoracotomy when epidural morphine rather than intravenous morphine is administered (48). However, lack of appropriate controls and influence of surgical stress limit the significance that can be attached to these studies. Despite these reservations, studies such as those of Popilskis et al (48), which correlate both subjective pain scores and endocrine responses, advance a persuasive case of the validity of pain scoring. Nevertheless, the difficulties highlighted by studies in man suggest that biochemical indices are unlikely to provide a reliable objective method of pain assessment in animals.

## **Pain Relief**

Leaving aside the problems of pain assessment, empirical treatment of presumed painful conditions will continue, and it is not unreasonable to assume that analgesic therapies shown to be effective in man are likely to also be effective in animals. Although the assessment of clinical efficacy may not have been completed, studies of novel analgesic compounds and delivery systems in animals have established their safety and efficacy in analgesiometric tests. Analgesics can be broadly divided into two groups, the opioids or narcotic analgesics and the non-steroidal anti-inflammatory drugs (NSAID) such as aspirin. Local anaesthetics can also be used to provide post-operative pain relief by blocking all sensation from the affected area. Suggested dose rates of analgesics are given in tables 1-4 [at the end of this article].



## **Clinical Use of Analgesics**

A number of clinical problems arise when analgesics are administered to control post-operative pain. The most important problem is the short duration of action of most of the opioid (narcotic) analgesics. Maintenance of effective analgesia with, for example, pethidine, may require repeated administration every 1-3 hours, depending upon the species. Continuation of such a regime overnight can cause practical problems. One method of avoiding this difficulty is to use buprenorphine as the analgesic, since there is good evidence in humans, rodents, rabbits and pigs that it has a duration of action for 6-12 hours (12, 16, 19, 25, 26). In clinical use in a wide range of animal species, it appears to provide effective pain relief to 6-12 hours. Its duration of action in the sheep appears to considerably less, although still of longer duration than pethidine and morphine (44).

An alternative approach is to adopt the well-established human clinical technique of administering analgesics as a continuous infusion. Infusions of analgesics have the advantage of maintaining effective plasma levels of the analgesic, thus providing continuous pain relief. This is in contrast to intermittent injections, where pain may return before the next dose of analgesic is administered. This technique obviously poses some methodological difficulties in animals, but if an indwelling catheter and harness and swivel apparatus are available, this can be arranged quite simply. In larger species (>3-4 kg body weight), a light weight infusion pump can be bandaged directly to the animal and continuous infusion made simply by means of a butterfly type needle anchored subcutaneously or intramuscularly. When analgesics are to be administered by continuous infusion, the infusion rate can be calculated from a knowledge of the pharmacokinetics of the analgesia to be used. If these data are not readily available, an approximation that appears successful in clinical use is as follows: calculate the total dose required over the period of infusion, reduce this by half and set the pump infusion rate accordingly; administer a single, normal dose of the drug as an initial loading dose and start the infusion. The rate can then be adjusted depending upon the animal's responses.

## **ALTERNATIVE ROUTES OF ADMINISTRATION**

Attempts to provide both longer periods of pain control and more effective analgesia have led to the development of alternative methods of drug delivery. The majority of these techniques have been developed in man and some have been used successfully in companion animals.

### **Epidural and Intrathecal Opioids**

Epidural and intrathecal opioids have been shown to have a prolonged effect in man, and to provide effective analgesia. In animals, clinical studies and experimental data indicate that the technique can be used in a number of species (14, 15, 45, 46, 48). Although used as a research tool in laboratory species (56), this route of administration has yet to be exploited as a means of controlling post-operative pain. The necessary techniques of epidural or intrathecal injection have been described in the rabbit (27, 30). In larger species such as the cat, dog, sheep, and pig, descriptions of the injection technique can be found in most veterinary anaesthesia texts and a number of other publications (eg., 32, 39).

### **Oral Administration**

The need for repeated injections of analgesics is time consuming and may be distressing to the animal, particularly smaller species which require firm physical restraint for an injection to be given safely and effectively. In addition, the need for repeated injections requires veterinary or other staff to attend the animal overnight. To circumvent this problem, the possibility of incorporating analgesics in food or water has been investigated (31). Long-term analgesia can be produced by this route. Kistler (31) reported that rats demonstrated analgesia for a two week period when

buprenorphine was administered continuously in the drinking water. Unfortunately, several practical problems limit the use of this technique. Some animals eat and drink relatively infrequently or may only do so in the dark phase of their photo period. In addition, food and water intake may be depressed following surgery, and this, coupled with wide individual variation in consumption, make routine application of the technique difficult. Finally, the high first-pass liver metabolism of opioids administered by the oral route requires that high dose rates are given, and this can represent a significant cost if all of the animals drinking water or food are medicated.

Administration of small quantities of medicated food does not avoid the need for repeated attendance overnight, but does remove the need for repeated subcutaneous or intramuscular injections in small rodents. Provision of analgesia with buprenorphine in flavoured gelatin, "Buprenorphine Jello"<sup>(47)</sup>, seems to be an effective means of providing post-operative pain relief. In our laboratory, we have noted that rats are initially cautious of jelly pellets, but once one pellet has been consumed, subsequent pellets are eaten as soon as they are offered. It is therefore advisable to commence administering pellets, which do not contain analgesic 2 to 3 days before surgery. After surgery, analgesic containing jelly can be given. The flavoured gelatin used is domestic fruit-flavoured jelly reconstituted at double the recommended strength.

Techniques for administration of food pellets at intervals to experimental animals are well-established, and it would be a relatively simple procedure to introduce an automated means of delivering pellets at appropriate time intervals. The technique could also be used with larger species and need not be restricted to opioids or, indeed, analgesics. Provided that the animal is eating or drinking, small quantities of highly palatable material could be provided at appropriate intervals. Simple timer devices to achieve this are already marketed for delayed feeding of pet dogs and cats.

As mentioned above, the administration of opioids by any route can be associated with the development of respiratory depression. It must be emphasized that this is rarely of clinical significance in animals, unless high doses of pure mu agonists (for example, fentanyl) are used. If respiratory depression occurs, it can be treated by the administration of the opiate antagonist drug, naloxone. Administration of naloxone will also reverse the analgesic effects of the opioid, and it may be preferable to correct the respiratory depression by the use of doxapram. Alternatively, if a mu opioid agonist such as morphine or fentanyl has been used, the respiratory depression can be reversed using nalbuphine or butorphanol, and some analgesia maintained because of the action of these latter two agents at kappa receptors. Repeated administration of these agents may be required, and the animal should be observed carefully for several hours to ensure that adequate respiratory function is maintained.

## **ADDITIONAL CONSIDERATIONS IN PAIN RELIEF**

Although the use of analgesic drugs remains the most important technique for reducing post-operative pain, the use of these drugs must be integrated into a total scheme for peri-operative care. Pain relief in the immediate recovery period can be provided by including an analgesic drug in any preanaesthetic medication. Alternatively, if a neuroleptanalgesic combination has been used to produce anaesthesia, it can be reversed by the use of buprenorphine, nalbuphine or butorphanol, rather than with naloxone. These agents have been shown not only to reverse the respiratory depressant effects of opioids such as fentanyl but, in contrast to naloxone, to provide effective prolonged analgesia (22, 34, 50).

The expertise of the surgeon can also greatly influence the degree of post-operative pain. Good surgical technique which minimizes tissue trauma and the prevention of tension on suture lines can considerably reduce post-operative pain. The use of bandages to pad and protect traumatized tissue must not be overlooked and forms an essential adjunct to the use of analgesic drugs.



Aside from measures directed towards alleviating or preventing pain, it is important to consider the overall care of the animal and the prevention of distress. Distress is used in this context to describe conditions which are not in themselves painful, but which are unpleasant and which the animal would normally choose to avoid. For example, recovering from anaesthesia on wet, uncomfortable bedding in a cold, unfamiliar environment would be likely to cause distress to many animals. It is essential to consider the methods described for the control of pain in conjunction with the techniques discussed earlier aimed at providing good post-operative care.

## RECOMMENDATIONS

It is difficult to make firm recommendations concerning which analgesics to use routinely, and how often to give them, because of the various factors outlined above. Nevertheless, as a general guide, the following techniques are used routinely in the author's research facility.

When carrying out any surgical procedure, buprenorphine is administered either pre-operatively or immediately following induction of anaesthesia, if a volatile anaesthesia is used. If neuroleptanalgesic regimens are used, or mu opioids are given as part of a balanced anaesthetic technique, then administration of buprenorphine is delayed until completion of surgery. If the procedure is relatively minor (for example, jugular or carotid cannulation) then only a single dose of analgesic is administered. In some circumstances a potent nonsteroidal anti-inflammatory drug (NSAID), such as flunixin or carprofen, may be used as an alternative to buprenorphine.

Following more invasive surgical procedures, such as laparotomy, orthopaedic surgery or craniotomy, opioid administration is continued for 24-48 hours. When undertaking major surgery, particularly in larger species when the degree of tissue trauma tends to be greater, analgesic administration may continue for 72 hours. Frequently, the regimen chosen consists of opioids (buprenorphine) in combination with an NSAID for 24-36 hours, followed by NSAID alone for a further 24-36 hours. (See tables 1-4 for suggested dose rates).

## CONCLUSIONS

Providing effective post-operative pain relief can have a dramatic effect on the speed with which animals return to normality following surgical procedures. It has been repeatedly demonstrated in humans that the provision of effective analgesia reduces the time taken for post-operative recovery (51). The provision of good post-operative care should be considered essential both because of a concern for the animal's welfare and also because it is good scientific practice.

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**Table 1. Suggested dose rates for non-steroidal anti-inflammatory drugs. Note that considerable individual and strain variation in response may be encountered, and it is therefore essential to assess the analgesic effects in each animal. Abbreviations: im=intramuscular, iv=intravenous, po=per os (by mouth), sc=subcutaneously, ?=approximate duration**

Drug	Mouse	Rat	Guinea Pig	Rabbit	Ferret
Aspirin	120mg/kg po	100 mg/kg po	87 mg/kg po	100 mg/kg po	200 mg/kg po
Carprofen		5 mg/kg sc		1.5 mg/kg po twice daily	
Diclofenac	8 mg/kg po	10 mg/kg po	2.1 mg/kg po		
Flunixin	2.5 mg/kg sc, im ?12 hourly	2.5 mg/kg sc, im ? 12 hourly		1.1 mg/kg sc, im ? 12 hourly	0.5-2 mg/kg sc 12-24 hourly
Ibuprofen	30 mg/kg po	15 mg/kg po	10 mg/kg im 4 hourly	10 mg/kg iv 4 hourly	
Indomethacin	1 mg/kg po	2 mg/kg po	8 mg/kg po	12.5 mg/kg po	
Ketoprofen		5 mg/kg po		3 mg/kg im	
Paracetamol (Acetominophen)	200 mg/kg po	200 mg/kg po			
Piroxicam	3 mg/kg po	3 mg/kg po	6 mg/kg po		



**Table 2. Suggested dose rates for non-steroidal anti-inflammatory drugs in laboratory animals. Note that considerable individual and strain variation in response may be encountered, and that it is therefore essential to assess the analgesic effects in each individual animal.**

Drug	Pig	Sheep	Primate	Dog	Cat
Aspirin		50-100 mg/kg po 6-12 hourly	20 mg/kg po 6-8 hourly	10-25 mg/kg po 8 hourly	10-25 mg/kg po every 48 hours
Carprofen	2-4 mg/kg iv or sc once daily	?	?	4 mg/kg iv or sc once daily 1-2 mg/kg bid po for 7 days	4 mg/kg iv or sc every 24 hours
Flunixin	1-2 mg/kg iv or sc once daily	2 mg/kg iv or sc once daily	2-4 mg/kg sc once daily	1 mg/kg iv or sc 12 hourly 1 mg/kg po for up to 3 days	1 mg/kg sc daily for up to 5 days
Ibuprofen				10 mg/kg po 24 hourly	
Ketoprofen				2 mg/kg sc, iv, or im once daily for up to 3 days 1 mg/kg po daily for 5 days	1 mg/kg sc once daily for up to 3 days 1 mg/kg po daily for 5 days
Paracetamol (Acetaminophen)				15 mg/kg po 6-8 hourly	Contraindicated
Piroxicam				300 µg/kg every 48 hours	

**Table 3. Suggested dose rates for opioid analgesics in common laboratory animals. Note that considerable individual and strain variation in response may be encountered, and that it is therefore essential to assess the analgesic effects in each individual animal.**

Drug	Mouse	Rat	Guinea Pig	Rabbit	Ferret
Buprenorphine	0.05-0.1 mg/kg sc 12 hourly	0.01-0.05 mg/kg sc, iv 8-12 hourly 0.1-0.25 mg/kg po 8-12 hourly	0.05 mg/kg sc 8-12 hourly	0.01-0.05 mg/kg sc, iv 8-12 hourly	0.01-0.03 mg/kg iv, im, sc 8-12 hourly
Butorphanol	1-5 mg/kg sc 4 hourly	2 mg/kg 4 hourly		0.1-0.5 mg/kg iv 4 hourly	0.4 mg/kg im 4-6 hourly
Morphine	2.5 mg/kg sc 2-4 hourly	2.5 mg/kg sc 2-4 hourly	2-5 mg/kg sc, im 4 hourly	2-5 mg/kg sc, im 2-4 hourly	0.5-5 mg/kg sc, im 6 hourly
Nalbuphine	4-8 mg/kg im ? 4 hourly	1-2 mg/kg im 3 hourly	1-2 mg/kg iv, im, ip	1-2 mg/kg iv 4-5 hourly	
Pentazocine	10 mg/kg sc 3-4 hourly	10 mg/kg sc 3-4 hourly		5-10 mg/kg sc, im, iv 4 hourly	
Pethidine (Meperidine)	10-20 mg/kg sc or im 2-3 hourly	10-20 mg/kg sc, im 2-3 hourly	10-20 mg/kg sc, im 2-3 hourly	10-20 mg/kg sc, im 2-3 hourly	5-10 mg/kg sc, im 2-4 hourly

**Table 4. Suggested dose rates for opioid analgesics in other animals. Note that considerable individual and strain variation in response may be encountered, and it is therefore essential to assess the analgesic effects in each animal.**

Drug	Pig	Sheep	Primate	Dog	Cat
Buprenorphine	0.005-0.02 mg/kg im, iv 6-12 hourly	0.005-0.01 mg/kg im, iv 4 hourly	0.005-0.01 mg/kg im, iv 6-12 hourly	0.005-0.02 mg/kg im, iv, sc 6-12 hourly	0.005-0.01 mg/kg iv, sc 8-12 hourly
Butorphanol			0.01 mg/kg iv ?3-4 hourly	0.2-0.4 mg/kg im, sc 3-4 hourly	0.4 mg/kg sc 3-4 hourly
Morphine	0.2-1 mg/kg im ?4 hourly	0.2-0.5 mg/kg im ?4 hourly	1-2 mg/kg im, sc 4 hourly	0.5-5 mg/kg im, sc 4 hourly	0.1 mg/kg sc 4 hourly
Nalbuphine				0.5-2.0 mg/kg im, sc 3-4 hourly	1.5-3.0 mg/kg iv 3 hourly
Oxymorphone				0.05-0.22 mg/kg im, iv, sc 2-4 hourly	0.2 mg/kg iv, sc
Pentazocine	2 mg/kg im, iv 4 hourly		2-5 mg/kg im, iv 4 hourly	2 mg/kg im, iv 4 hourly	
Pethidine (Meperidine)	2 mg/kg im, iv 2-4 hourly	2 mg/kg im, iv 2-4 hourly	2-4 mg/kg im, iv 2-4 hourly	10 mg/kg im 2-3 hourly	2-10 mg/kg im, sc 2-3 hourly

# Guidelines for the Euthanasia of Mouse and Rat Fetuses and Neonates

These guidelines were revised and reapproved on November 10, 1998 by the National Institutes of Health Animal Research Advisory Committee and may be found at <http://oacu.od.nih.gov/ARAC/euthmous.htm>

The Report of the AVMA Panel on Euthanasia does not provide specific recommendations for the euthanasia of prenatal or neonatal animals. The following guidelines are suggested to assist individual Animal Care and Use Committees at the NIH in reviewing proposals which involve the use of rodent fetuses or neonates.

## Fetuses:

- a. Fetuses up to 14 days in gestation: Neural development at this stage is minimal and pain perception is considered unlikely. Euthanasia of the mother or removal of the fetus should ensure rapid death of the fetus due to loss of blood supply and non-viability of fetuses at this stage of development.
- b. Fetuses 15 days in gestation to birth: The literature on the development of pain pathways suggests the possibility of pain perception at this time. Whereas fetuses at this age are not sensitive to inhalant anesthetics, euthanasia may be induced by the skillful injection of chemical anesthetics. Decapitation with surgical scissors, cervical dislocation, or rapid freezing (immersion in liquid nitrogen) are acceptable physical methods of euthanasia. When chemical fixation of the whole fetus is required, fetuses should be anesthetized prior to immersion in or perfusion with fixative solutions. Anesthesia may be induced by hypothermia (1) of the fetus, by injection of the fetus with a chemical anesthetic, or by deep anesthesia of the mother with a chemical agent that crosses the placenta, e.g., pentobarbital. The institute veterinarian should be consulted for considerations of fetal sensitivity to specific anesthetic agents. When fetuses are not required for study, the method chosen for euthanasia of a pregnant mother must ensure rapid death of the fetus.

## Neonates:

- a. Up to 14 days of age: Acceptable methods for the euthanasia of neonatal mice and rats include: injection of chemical anesthetics (e.g., pentobarbital), decapitation, or cervical dislocation. Additionally, these animals are sensitive to inhalant anesthetics; e.g., methoxyflurane (used with appropriate safety considerations). Immersion in liquid nitrogen may be used only for newborns; pups older than one day should be anesthetized prior to freezing with liquid nitrogen. Similarly, anesthesia should precede immersion or perfusion with chemical fixatives. Anesthesia may be induced by inhalant or injectable anesthetics; the institute veterinarian should be consulted for appropriate agents and dosages. Alternatively, when adequately justified, hypothermia<sup>1</sup> may be used to induce anesthesia in pups six days of age or less.
- b. Older than 14 days: Follow guidelines for adults.

In all cases, the person performing the euthanasia must be fully trained in the appropriate procedures.

(1) Phifer CB, Terry LM. 1986. Use of hypothermia for general anesthesia in preweanling rodent. *Physiol & Behav* 38:887-890.





# Humane Endpoints and Pain Management Bibliography

- Amyx, H.L. (1987). **Alternatives to the LD-50 in infectious disease studies.** *Scientists Center for Animal Welfare Newsletter* 9(4): 1-2.  
NAL call number: QL55 N48  
Descriptors: reducing animal numbers, preventing pain, infectious dose 50, incubation time interval assay, alternatives, humane endpoints, infectious diseases, titration of infectious agents in live animals, diagnostic tools, clinical signs of disease.
- Amyx, H.L. (1987). **Control of animal pain and distress in antibody production and infectious disease studies.** *JAVMA* 191(10): 1287-1289.  
NAL call number: 41.8 Am3  
Descriptors: Freund's complete adjuvant, alternative adjuvants, minimization of side-effects of Freund's by careful control of injection quantity and injection site selection, rabbits, inappropriate to use Freund's in feet of rabbits, rodent footpad injections, ascites, pristane, restraint methods, animal care personnel, principles for control of pain and distress, humane endpoints, monitoring health of animals, euthanasia, analgesics, experimental design, rodents, dogs, cats, primates.
- Blogg, S.L., P.P. Townsend, P.J. Butler, and E.W. Taylor (1998). **A method of anaesthesia and post-operative care for experimental procedures in avian species.** *Animal Technology* 49(2): 101-109.  
NAL call number: QL55 I5  
AB- This paper describes a successful method of anaesthesia for prolonged and/or invasive avian surgery, along with an appropriate protocol for post-operative care. These methods were determined during a neuroanatomical study of two species of bird, the tufted duck (*Aythya fuligula*) and the domestic duck (*Anas platyrhynchos*), as part of an ongoing scientific study. Descriptions of current, relevant techniques of anaesthesia suitable for this study, were not readily available, therefore we felt that details of our methods would be a valuable contribution to this field. A standard operating procedure for use in similar studies and an example of an avian post-operative score sheet are outlined.
- Browder, E.J. (1995). **Death as an endpoint.** In *Current Issues and New Frontiers in Animal Research*, K.A.L. Bayne, M. Greene, and E.D. Prentice, (eds.), Greenbelt, Maryland: Scientists Center for Animal Welfare, pp. 25-29.  
NAL call number: HV4913 C87 1995  
Descriptors: LD50, scientific justification, humane endpoints, assessment of animals, temperature drop, rectal temperature, IACUC responsibilities, investigator responsibilities, animal care staff responsibilities, funding agency responsibilities, data collection, assessment of pain and distress, selected criteria for euthanasia of moribund animals.
- Canadian Council on Animal Care (1999). **CCAC guidelines on: Choosing an appropriate endpoint in experiments using animals for research, education, and testing.** Ottawa, Ontario, Canada: Canadian Council on Animal Care. Available at <http://www.ccac.ca/english/gdlines/endpts/app1to8.htm>  
Descriptors: animal observation, significant indicators of pain and distress, scoring significant behavioral and physiological observations to set endpoints, pilot studies to determine appropriate endpoint, determining frequency of observations, defining responsibility for observations, training personnel in clinical animal observations, role of the IACUC, monoclonal antibody production, cancer research, toxicology, pain research, infectious disease studies, vaccine trials, animal models with potential for significant levels of pain and distress, species specific signs of pain and distress, information sources, understanding normal animal behavior, recognition and assessment of pain and distress,

laboratory animals, fish, farm animals, examples of observational checklists used to determine endpoints.

Coenen, A.M.L., W.H.I.M. Drinkenburg, R. Hoenderken, and E.L.J.M. van Luijtelaar (1995).

**Carbon dioxide euthanasia in rats: oxygen supplementation minimizes signs of agitation and asphyxia.** *Laboratory Animals* 29(3): 262-268.

NAL call number: QL55 A1L3

Descriptors: experimental methods, behavior, electroencephalogram (EEG), electrocardiogram (ECG), effect of method—animals added to a box: completely filled with CO<sub>2</sub>, into which CO<sub>2</sub> was streamed at a high flow rate, into which CO<sub>2</sub> was streamed at a low flow rate, into which a mixture of CO<sub>2</sub> and O<sub>2</sub> was streamed at a fast rate, negative aspects of CO<sub>2</sub> euthanasia can be prevented by an additional supply of oxygen.

Close, B., K. Banister, V. Baumans, E-M. Bernoth, N. Bromage, J. Bunyan, W. Erhardt, P.

Flecknell, N. Gregory, H. Hackbarth, D. Morton, and C. Warwick (1997). **Working party report: Recommendations for euthanasia of experimental animals: Part 2.** *Laboratory Animals* 31(1): 1-32.

NAL call number: QL55 A1L3

Descriptors: This document was prepared for the European Commission to be used with Directive 86/609/EEC on animal welfare, excellent review of methods of euthanasia for fish, amphibians, reptiles, birds, rodents, rabbits, carnivores (dogs, cats, ferrets), large mammals (pigs, sheep, goats, cattle, horses), nonhuman primates, less commonly used species, each section includes information on overview of the species, recognition and confirmation of death, how to euthanize larvae or embryos, physical methods, chemical methods, unacceptable methods of euthanasia.

Cunningham, J.J. and D.C. Priddy (1999). **A low-cost chamber for rodent CO<sub>2</sub> euthanasia.** *Lab Animal* 28(2):

NAL call number: QL55 A1L33

Descriptors: euthanasia, technique, low-cost method, humane.

Danneman, P.J., S. Stein, and S.O. Walshaw (1997). **Humane and practical implications of using carbon dioxide mixed with oxygen for anesthesia or euthanasia of rats.** *Laboratory Animal Science* 47(4): 376-385.

NAL call number: 410.9 P94

AB: A series of studies was undertaken to determine whether CO<sub>2</sub> can be used as a humane as well as practical agent for euthanasia or anesthesia of rats. Human volunteers rated the degree of discomfort associated with breathing 50 to 100% CO<sub>2</sub> mixed with oxygen. Increasing concentrations of CO<sub>2</sub> were judged as progressively more noxious, from "highly unpleasant" for 50% CO<sub>2</sub> to "painful" for 100% CO<sub>2</sub>. The practical aspects of anesthesia and euthanasia with 50 to 100% CO<sub>2</sub> were studied, using male Sprague Dawley rats. Time to anesthesia and death were inversely related to CO<sub>2</sub> concentration, as were the frequency and severity of adverse reactions, including seizures and hemorrhaging from the nose. The severity of edema and hemorrhage, which were observed on histologic examination of the lungs of all rats euthanized with CO<sub>2</sub>, were greatest in the animals exposed to the lowest concentrations. There were no significant effects of CO<sub>2</sub> concentration on time to recumbency or recovery, and there were no significant effects of precharging versus not precharging the chamber on any of the parameters studied. It was concluded that, although CO<sub>2</sub> can be used in a humane manner, the concentrations that are least likely to cause pain and distress are associated with the longest times to anesthesia and death, highest incidence of unwanted side effects, and most severe histologic changes in the lungs. Acceptably humane and reasonably practical euthanasia or anesthesia can be achieved using a nonprecharged chamber and a low gas flow rate so that conscious animals are never exposed to CO<sub>2</sub> concentrations >70%.

- Flecknell, P. (1997). **Avoidance and alleviation of pain and distress.** In *Animal alternatives, welfare, and ethics, Proceedings of the 2nd World Congress on Alternatives and Animal Use in the Life Sciences, held in Utrecht, the Netherlands, 20-24 October 1996*, L.F.M. Zutphen and M. Balls (eds.), Amsterdam, New York: Elsevier, pp. 241-245.  
NAL call number: QL1 D48 v.27  
Descriptors: pain assessment, animal behavior, terminal anesthesia, analgesics, anxiolytics, humane endpoints, housing, animal husbandry.
- Flecknell, P. (1997). **Medetomidine and atipamezole: Potential uses in laboratory animals.** *Lab Animal* 26(2): 21-25.  
NAL call number: QL55 A1L33  
Descriptors: pharmacology, clinical uses, sedation, anesthesia, tables of suggested doses for cats, dogs, gerbils, guinea pigs, ferrets, hamsters, mice, pigs, rabbits, rats, sheep, marmosets, anesthetic combinations.
- Foltz, C.J. and M. Ullman-Cullere (1999). **Guidelines for assessing the health and condition of mice.** *Lab Animal* 28(4): 28-32.  
NAL call number: QL55 A1L33  
Descriptors: transgenic mice, knockout mice, potentially debilitating phenotypes, humane endpoints, monitoring criteria, communications between veterinary staff and investigators, body condition scoring, health guidelines, barbering, fighting, malocclusion, rectal prolapse, tumors and masses, ulcerative dermatitis, vaginal or uterine prolapse, subtle health problems – activity/behavior, anemia, dehydration, diarrhea, hypothermia, preputial or vaginal discharge, additional health problems–abnormal breathing, abnormal locomotion, eye abnormality, head tilt, hyperactivity, lethargy, paresis, paralysis, ruffled fur, tremors.
- Gentle M.J. (1992). **Pain in birds.** *Animal Welfare* 1(4): 235-247.  
NAL call number: HV4701 A557  
Descriptors: poultry, recognition and assessment of pain, nociceptors, behavioral and physiological responses to nociceptive stimulation, pain following trauma, animal welfare, debeaking, analgesics, pain, trauma, reviews.
- Hamm, T.E. Jr. (1995). **Proposed institutional animal care and use committee guidelines for death as an endpoint in rodent studies.** *Contemporary Topics in Laboratory Animal Science* 34 (3): 69-71.  
NAL call number: SF405.5.A23.  
Descriptors: laboratory animals, endpoints, animal welfare, committees, guidelines, rodents, death, regulations.
- Hellyer, P. (1998). **American College of Veterinary Anesthesiologists' position paper on the treatment of pain in animals.** *Journal of the American Veterinary Medical Association* 213 (5): 628-630.  
NAL call number: 41.8 Am3  
Descriptors: animal welfare, pain, symptoms, treatment, anesthesia.
- Jones, D.M. (1999). **Carbon dioxide induced anesthesia has no effect on brain biogenic amine concentrations in mice.** *Laboratory Animal Science* 49(3): 316-318.  
NAL call number: 410.9 P94  
Descriptors: humane death, norepinephrine, dopamine, serotonin, cortex, hippocampus, striatum, cerebellum, decapitation.
- Kallman, R.F., J.M. Brown, J. Denekamp, R.P. Hill, J. Kummermehr, and K.-R. Trott (1985). **The use of rodent tumors in experimental cancer therapy. Conclusions and recommendations from an international workshop.** *Cancer Research* 45: 6541-6545.



NAL call number: 448.8 C16

Descriptors: tumor/host systems, model systems, tumor immunogenicity, host animals, assay procedures, tumor growth delay assay, cellular survival assays following excision, experimental variables that can affect assay procedures or the interpretation of results, animal health and husbandry, site of tumor implantation, tumor size, stress, anesthesia, hypothermia, experimental design, radiation exposure time, cell cycle effects, drug resistance, combined modality experiments, models for adjuvant therapy, ethical principles, tumors should not exceed 10 percent of body weight.

Kastello, D.A. (1990). **Recognition and alleviation of pain and distress.** *Symposium: Animal Welfare Compliance for Study Directors* Orlando, Florida: American College of Toxicology. NAL call number: Videocassette no. 968

Descriptors: study director, veterinarian, ACUC, pain, humane endpoints.

Keefe, F.J., R.B. Fillingim, and D.A. Williams (1991). **Behavioral assessment of pain: Nonverbal measures in animals and humans.** *ILAR News* 33(1-2): 3-13.

NAL call number:

Descriptors: excellent review of pain induction methods for analgesia testing, tail flick, hot plate, flinch-jump, pinch, formalin, chronic pain paradigms, pain measurement methods, quantification of presence of analgesia, animals, humans, devices, observation methods.

Koolhaas J.M., V. Baumans, H.J.M. Blom, D. Holst von, P.J.A. Timmermans, P.R. Wiepkema, D. Von Holst, L.F.M. Zutphen van (ed.), V. Baumans (ed.), and A.C. Beynen (1993).

**Behaviour, stress and well-being.** In *Principles of laboratory animal science: A contribution to the humane use and care of animals and to the quality of experimental results*. L.F.M. van Zutphen, V. Baumans, and A.C. Beynen (eds.), Amsterdam: Elsevier Science Publishers, pp. 75-99.

NAL call number: QL55 P762 1993

Descriptors: laboratory animals, animal experiments, adaptation, learning, environment, physiology, animal behaviour, animal welfare, stress, homeostasis, phylogeny, learning, ontogeny, interaction between animal and its environment, interaction between environment and physiology, autonomic nervous system, neuroendocrine system, functional significance of physiological stress responses, pathophysiology, well-being .

Kort, W.J., J.M. Hekking-Weijma, M.T. TenKate, V. Sorm, and R. van Strik (1998). **A microchip implant system as a method to determine body temperature of terminally ill rats and mice.** *Laboratory Animals* 32(3): 260-269.

NAL call number: QL55 A1L3

AB- *Klebsiella pneumoniae* was inoculated intratracheally into rats and mice, and the temperature of the animals was recorded twice daily using microchip transponders (ELAMS) implanted either s.c. or i.p. The microchip temperatures were compared with rectal temperatures taken at the same time. The results showed that ELAMS was easy to operate and there were no important drawbacks in the use of the system were observed. The temperatures measured by the transponders implanted s.c. and i.p. did not differ significantly from rectal temperatures. In 2 out of 3 experiments on rats, it was shown that when the temperatures reached values below 36 °C, the median survival time of the animals was 24 h. In an experiment on mice, the same median survival time was observed at 36 °C. In 1 experiment using rats, however, the disease was so acute that death occurred before any temperature drop. It is suggested that when a 36 °C cutoff point is used instead of the time of death in this particular animal model, the statistical analysis is not altered, and it may spare animals further suffering for approximately 24 h. It is concluded that the ELAMS system of monitoring body temperature is simple and relatively stress free for laboratory animals. Descriptors: body temperature, monitoring, microchips, transponders, animal welfare, experimental infectious diseases.

Liles, J.H. and P.A. Flecknell (1992). **The use of non-steroidal anti-inflammatory drugs for relief of pain in laboratory rodents and rabbits.** *Laboratory Animals* 26(4): 241-255.

NAL call number: QL55 A1L3

Descriptors: classification of non-opioid non-steroidal analgesics, pharmacology of NSAIDs, assessment of analgesic efficacy, thermal stimulus, electrical stimulus, chemical methods, mechanical forces, edema tests, analgesimetry and clinical pain, effective analgesic and lethal doses of NSAIDs in mice, adverse effects of NSAIDs and selection of dose rates, analgesic, anti-inflammatory, and lethal doses in rats, ulcerogenic doses in rats, use of NSAIDs in humans and animals, suggestions for uses in laboratory animals.

Louie, A., W. Liu, Q.F. Liu, A.C. Sucke, D.A. Miller, A. Battles, and M.H. Miller (1997).

**Predictive value of several signs of infection as surrogate markers for mortality in a neutropenic guinea pig model of *Pseudomonas aeruginosa* sepsis.** *Laboratory Animal Science* 47(6): 617-623.

NAL call number: 410.9-P94

AB-Infected, neutropenic animals are used as experimental models to evaluate the relative efficacies of antimicrobial agents and host-pathogen-antibiotic interactions. In the past, these models used death as the study end point. Because of the concern about use of death as an end point, we evaluated the accuracy with which various signs of infection predicted mortality in a neutropenic guinea pig model of treated and untreated *Pseudomonas aeruginosa* sepsis. The potential surrogate markers studied included ruffled fur, respiratory distress, diarrhea, hunched posture, lethargy, abnormal neurologic movements (twitching, paralysis of a limb), inappetence for > 48 h, the inability to ambulate, and the inability of a supine animal to stand. In addition, we evaluated whether percentage of weight loss or change in daily food and water consumption were predictive of mortality. Animals were inspected for these signs at least every 4 h during the day and every 8 h in the evening. In treated and untreated animals, 100% of subjects that were unable to ambulate or to rise from the supine position died (positive predictive value for death was 100% for either sign). Guinea pigs that could not rise from a supine position expired between 1 and 8 h after this sign was observed. Those that could not ambulate died between 4 and 40 h after that sign was observed. In treated, and untreated animals, none of the survivors manifested either sign of disease (100% specificity for each sign). However, 59% of untreated and 69% of treated animals that were ambulatory were found dead at the next observation period, underscoring the rapidity with which this infection progresses to death when it enters its final stage. No other signs of infection distinguished animals that survived or died. Thus, the inability of neutropenic, infected guinea pigs to rise from a supine position and the inability to ambulate were the only signs that accurately predicted death and, therefore, are the only signs that can be used as surrogates for death in this experimental model of *P. aeruginosa* sepsis.

DE: animal models, *Pseudomonas aeruginosa*, sepsis, surrogate markers, mortality prediction, weight losses, food intake, water intake, imipenem, tobramycin, ceftazidime, antibiotics, humane endpoints.

Montgomery, C.A. (1987). **Control of animal pain and distress in cancer and toxicological research.** *JAVMA* 191(10): 1277-1281.

NAL call number: 41.8 Am3

Descriptors: experimental design, choice of rodent strain, statistical assessment of studies, animal husbandry and disease control, housing and bedding, conduct and interpretation of a study, selected clinical observations used in toxicologic studies, route of chemical administration, selected criteria for euthanasia of moribund animals, veterinary care, training.

Morton, D.B. (1998). **The recognition of adverse effects on animals during experiments and its use in the implementation of refinements.** In *Proceedings of the Joint ANZCCART/NAEAC conference on Ethical Approaches to Animal-based Science*, D. Mellor, M. Fisher, and G. Sutherland (eds.), Adelaide, Australia and Wellington, New Zealand: ANZCCART, pp. 61-67.



- Morton, D.B. (1998). **The use of score sheets in the implementation of humane end points.** In *Proceedings of the Joint ANZCCART/ NAEAC conference on Ethical Approaches to Animal-based Science*, D. Mellor, M. Fisher, and G. Sutherland (eds.), Adelaide, Australia and Wellington, New Zealand: ANZCCART, pp. 75-82.
- Morton, D.B. (1997). **A scheme for the recognition and assessment of adverse effects in animals.** In *Animal alternatives, welfare, and ethics, Proceedings of the 2nd World Congress on Alternatives and Animal Use in the Life Sciences, held in Utrecht, the Netherlands, 20-24 October 1996*, L.F.M. Zutphen and M. Balls (eds.), Amsterdam, New York: Elsevier, pp. 235-240.  
NAL call number: QL1 D48 v.27  
Descriptors: husbandry and experimental techniques, score sheets, body weight, activity, temperature, vocalization, abdominal distension, palpate, sunken eyes, dehydration, breathing, observation, humane endpoints.
- Morton, D.B. and Griffiths, P.H.M. (1985). **Guidelines on the recognition of pain, distress, and discomfort in experimental animals and an hypothesis for assessment.** *Veterinary Record* 116(16): 431-436.  
NAL call number: 41.8 V641  
Descriptors: signs of pain, distress, and discomfort, aids in their interpretation, appearance, food and water intake, behavior, clinical signs, cardiovascular, respiratory, digestive, nervous and musculoskeletal, temperature, edema, swelling, discharges, urinary changes, quantitative assessment of pain, distress, and discomfort, bodyweight, relationships between signs and degree of pain, distress, and discomfort, interpretation of scoring from an overall assessment, species specific clinical signs indicating pain, rats, mice, rabbits, guinea pigs, dogs, cats, primates.
- National Research Council (1992). **Recognition and Alleviation of Pain and Distress in Laboratory Animals.** Washington, D.C.: National Academy Press, 137 p.  
NAL call number: SF996.5 R43 1992  
Descriptors: biologic importance of pain and distress, stressors, distress models, basis of pain, basis of stress and distress not induced by pain, recognition and assessment of pain, stress and distress, control of pain, control of stress and distress, euthanasia.
- Phifer, C.B. and L.M. Terry (1986). **Use of hypothermia for general anesthesia in preweanling rodents.** *Physiology and Behavior* 38(6): 887-890.  
NAL call number: QP1 P4  
Descriptors: rationale and background, techniques used to induce hypothermia, deep hypothermia for surgical manipulations, moderate hypothermia as adjunct, applications.
- Raufer B. and M. Miller (1997). **Euthanasia: an animal-care protocol.** *Pork* 17(2): 32-37.  
Descriptors: techniques, pain, euthanasia, animal welfare.
- Redgate, E.S., M. Deutsch, and S.S. Boggs. **Time of death of CNS tumor-bearing rats can be reliably predicted by body weight-loss patterns.** *Laboratory Animal Science* 41(3): 269-273.  
NAL call number: 410.9 P94  
Descriptors: ACUC, central nervous system, antineoplastic drug, moribund state, alternative to death as endpoint, tumor growth, neoplasms.
- Rockwell, S. (1987). **Maintenance of tumor systems and appropriate treatment techniques for experimental tumors.** In *Rodent Tumor Models in Experimental Cancer Therapy*, R.F. Kallman, ed., Elmsford, New York: Pergamon Press, pp.29-36.  
NAL call number: RC261 A2R62

Descriptors: choice and maintenance of animals, effect of pathogenic microorganisms, contamination of personnel, appropriate treatment techniques, choice of appropriate tumor, effects of anesthesia and restraint, tumor size-a 200mm<sup>2</sup> (about 3/8 inch X 3/4 inch) tumor in a 20-25 (about 1 ounce) gram mouse is roughly equivalent to a 600 gram (1 pound 5 ounces) tumor in a 60-75 kg (132-165 pounds) patient, effects of stress, induction of tumor hypoxia, host-mediated effects.

Rollin, B.E. (1997). **Pain and ideology in human and veterinary medicine.** *Seminars in Veterinary Medicine and Surgery (Small Animals)* 12(2): 56-60.  
Descriptors: animal welfare, philosophy, analgesics, anesthetics, pain.

Siems, J.J. and Allen, S.D. (1989). **Early euthanasia as an alternative to death in chronic infectious disease studies using a systemic *Candida albicans* model.** *Abstracts of the 89<sup>th</sup> Annual Meeting of the American Society for Microbiology* 1989: 81 (B-304).  
NAL call number: QR1 A5  
Descriptors: humane endpoints, predicting time of animal's death, multiple regression analysis, use of variables, weight loss, temperature drop, tenting-an indicator of dehydration, ataxia, rough hair coat, assessment of animal conditions throughout experiment, prevention of post-mortem change of tissues and body fluids.

Shipp, K. and B.D. Woodward (1998). **A simple exsanguination method that minimizes acute pre-anesthesia stress in the mouse: evidence based on serum corticosterone concentrations.** *Contemporary Topics in Laboratory Animal Science* 37(5): 73-77.  
NAL call number: SF405.5.A23  
Descriptors: stress, anesthesia, corticosterone, blood collection, inhalation anesthetics, animal welfare, carbon dioxide.

Soma, L.R. (1987). **Assessment of animal pain in experimental animals.** In *Effective Animal Care and Use Committees*, F.B. Orlans, R.C. Simmonds, and W.J. Dodds (eds.), 71-74. Special Issue of *Laboratory Animal Science*, Bethesda, Maryland: Scientists Center for Animal Welfare, pp.71-74.  
NAL call number: QL55 E4  
Descriptors: pain responses of animals, surgical procedures, postoperative pain, procedures likely to require analgesics or sedatives, clinical assessment of pain, chronic pain, chronic illness.

Soothill, J.S., Morton, D.B., and Ahmad, A. (1992). **The HID-50 (hypothermia inducing dose 50): An alternative to the LD-50 for measurement of bacterial virulence.** *International Journal of Experimental Pathology* 73: 95-98.  
Descriptors: rectal temperature, temperature drop, prediction of time of death, humane endpoint, euthanasia, alternatives.

Svendsen, P. and C. Rasmussen (1998). **Anaesthesia of minipigs and basic surgical techniques.** *Scandinavian Journal of Laboratory Animal Science* 25(SUPP 1): 31-43.  
NAL call number: QL55 S322  
Descriptors: miniature pigs, surgery, anesthesia, methods.

Tomasovic, S.P., Coghlan, L.G, Gray, K.N., Mastromarino, A.J., and Travis, E.L. (1988). **IACUC evaluation of experiments requiring death as an endpoint: A cancer center's recommendations.** *Lab Animal* 17(1): 31-34.  
NAL call number: QL55 A1L33  
AB- IACUCs in some institutions face special problems with protocols in which death is the required end point. A possible alternative in some cases may be euthanasia when the animals become moribund.



Townsend, P. (1993). **Control of pain and distress in small laboratory animals.** *Animal Technology* 44(3): 215-223.

NAL call number: QL55 I5

AB-The prevention and alleviation of pain and distress in laboratory animals is presented as a strategy incorporating management, animal husbandry and scientific techniques, involving all those concerned with animal care and use, including animal technicians, veterinary surgeons and scientists. The paper identifies causes of pain and distress throughout the experimental animals life and attempts to highlight practical ways of preventing or, if this is not possible, alleviating any pain or distress which the animal may endure. All of the strategies involve making the laboratory animal the focus of concern when designing experimental schedules, as the prevention of pain and distress is the first step to producing good science.

Descriptors: distressful situations-fear, loneliness, boredom, preemptive control-planning for avoidance, refinement of techniques to minimize discomfort, alleviation of pain, anesthesia, analgesia, review of drugs, humane endpoints, euthanasia, examples of score sheets.

Toth, L.A. (1997). **The moribund state as an experimental endpoint.** *Contemporary Topics in Laboratory Animal Science* 36(3): 44-48.

NAL call number: SF405.5.A23.

Descriptors: pain scoring, distress, suffering in animals, experimental paradigms, use of objective information to predict death, humane endpoints, use of experimentally relevant clinical signs, body weight, body temperature, euthanasia.

Ullman-Culleré, M.H. and C.J. Foltz (1999). **Body condition scoring: A rapid and accurate method for assessing health status in mice.** *Laboratory Animal Science* 49(3): 319-323.

NAL call number: 410.9 P94

Descriptors: noninvasive methods, criteria for euthanasia, emaciation, underconditioned, well-conditioned, overconditioned, obese, tumors, aging studies.

**United Kingdom Co-ordinating Committee on Cancer Research (UKCCCR) Guidelines for the Welfare of Animals in Experimental Neoplasia (Second Edition) (1998).** *British Journal of Cancer* 77(1): 1-10.

Descriptors: animal welfare; experimental neoplasms, research design, analgesia, animal growth and development, disease models, gene therapy, neoplasm transplantation, neoplasms physiopathology, neoplasms, therapy, humane endpoints.

Van Loo, P.L.P., L.A. Everse, M.R. Bernsen, V. Baumans, L.J. Hellebrekers, C.L.J.J. Kruitwagen, and W.den Otter (1997). **Analgesics in mice used in cancer research: reduction of discomfort?** *Laboratory Animals* 31(4): 318-325.

NAL call number: QL55 A1L3

Descriptors: animal behavior, exploration, grooming, posture, food and water consumption, buprenorphine administered in Jello, chronic pain, advanced tumors, study could not document a positive effect of buprenorphine on discomfort, possible explanations are examined.

Wallace, J., J. Sanford, M.W. Smith, and K.V. Spencer (1990). **The assessment and control of the severity of scientific procedures on laboratory animals.** *Laboratory Animals* 24: 97-130.

NAL call number: QL55 A1L3

Descriptors: definitions of severity, assessment of severity, components, index of severity, identifying and scoring pain, control of the severity of scientific procedures, development of a program for control, management practices, training, animal husbandry, humane and experimental endpoints, behavioral changes, psychosocial influences, diseases, euthanasia, sensitivity of tissues and organs to challenges, recognition and assessment of pain and distress, potential responses and physiological signs are provided for the following species: mouse, guinea pig, rabbit, golden hamster, and gerbil, comprehensive indices of severity of

scientific procedures are provided for administration of substances, collection of tissue and body fluids, surgical techniques, and restraint.

Wright, A.J. and R.J. Phillpotts (1998). **Humane endpoints are an objective measure of morbidity in Venezuelan encephalomyelitis virus infection of mice.** *Archives of Virology* 143(6): 1155-1162.

NAL call number: 448.3 Ar23

Descriptors: acute infection, symptoms, clinical aspects, animal welfare, equine encephalomyelitis virus, humane endpoints.

## Useful World Wide Web Sites

### **American Veterinary Medical Association Panel on Euthanasia Report, 1993**

<http://www.nal.usda.gov/awic/pubs/noawicpubs/avmaeuth.htm>

Euthanasia methods approved by the AVMA and referenced by USDA and PHS.

### **Assessment of Pain and Distress in Laboratory Animals**

<http://www.ahc.umn.edu/rar/pain&distress.html>

Provided by Research Animal Resources, University of Minnesota

### **Compilation of Literature on the Assessment of Animal Welfare and Animal Distress**

<http://www.vetinfo.demon.nl/aw/>

Extensive bibliography and links to full-text documents related to the assessment of pain in animals, animal welfare, and animal distress. Produced by dr. J.D. Kuiper, Department of Laboratory Animal Sciences, Utrecht University, Utrecht, The Netherlands, and Tim Allen, Animal Welfare Information Center, U.S. Department of Agriculture, Beltsville, Maryland.

### **Endpoints for Research Projects in Animals That Have the Potential To Cause Severe Or Chronic Pain or Distress**

<http://www.emory.edu/WHSC/MED/IACUC/endpoint.htm>

Provided by Emory University

### **Guidelines For Endpoint Monitoring And Humane Termination**

<http://www-portfolio.stanford.edu/103951>

Provided by the Dean of Research, Stanford University

### **Guidelines on Death as an Endpoint**

<http://www2.ec.hscsyrc.edu/dlar/deathend.htm>

Provided by Department of Laboratory Animal Resources at State University of New York-Health Sciences Center in Syracuse, NY.

### **IACUC and Pain-Related Internet Resources**

<http://netvet.wustl.edu/pain.htm>

Approximately 400 web-based resources relevant to pain or IACUC's are referenced. This collection of links attempts to provide those interested with an overview of some of the best information currently available on the Internet. The categories of resources listed include: major neuroscience directories, resource references, journals, meetings, government agencies and regulations, anesthesia and analgesia, academic departments, institutional animal care and use committees, animal behavior, ethics and alternatives to animal testing, commercial resources, as well as pain societies and animal research organizations.



# Farm Animals







# Welfare Concerns for Farm Animals Used in Agricultural and Biomedical Research and Teaching

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## Introduction

Issues of animal welfare are often thought to be easily dissipated by the production of scientific arguments and evidence. However, animal welfare is not only a scientific issue. Politics, philosophy and ethics, and aesthetics can influence societal expectations concerning the use, care and treatment of animals (2). Because of the multiple influences that come to bear on the issue, it is nearly impossible to reach agreement on a precise definition of animal welfare. However, there seems to be a general consensus that there are two central themes, the state of the animal itself and broader sociological factors. An approach used within the scientific community is to use the term *animal well-being* when referring to the actual welfare status of the animal, and *animal welfare* when referring to broader sociological and ethical concerns (9,5,6). When encountering concerns regarding farm animal use in research and teaching, there is a need to address the broader sociological and ethical expectations in addition to the scientific.

## Agricultural Research and Teaching

Farm animals used for agricultural research require strict attention to their care, husbandry and maintenance of protocol requirements under a variety of conditions. The research environment may vary from fairly extensive (e.g. grazing study) to very intensive (e.g. metabolism trial). It is expected that the research animals will not be subjected to unnecessary pain or distress and will be observed for the development of signs of distress. Social (e.g. isolation) or physiological (e.g. sensory) deprivation tend to raise concerns and questions about the necessity of the procedure and potential benefits of the research. Agriculture is typically perceived as an applied science and when research protocols require greater manipulation (e.g. invasive procedures) questions arise concerning the potential application of results and the skill of the researcher(s) involved. For example, field or standing surgery often poses questions regarding potential harm to the animal due to lack of aseptic conditions or adequate pain control. Other surgical procedures such as fistulation, laparotomies, cannulation, etc. are sometimes performed by persons other than veterinary surgeons (e.g. trained Ph.D. or graduate students) which presents issues concerning proper training and oversight (14). Pre- and post-operative care, pain recognition, and management are critical to the animal well-being. Handling, equipment use and condition, and methods that are current with good practice are important from both a research and welfare perspective (7). Concerns often arise when observation notes deficiencies in any of the area's mentioned above and effects on animals are perceived.

Teaching in agricultural schools and colleges also presents concerns for the animals and the safety of the students. A wide variety of teaching activities occur from basic "hands-on" experience such as leading animals to fairly technical physiological laboratories. Handling animals that are relatively large requires that instructors are knowledgeable about the specie with which they are working and safety precautions that need to be considered to protect students and animals. Concerns

arise regarding the instructors competency in animal behavior, husbandry, handling methods, and technical skills. Also of concern are suitability of teaching facilities, holding quarters, transportation to and from instructional sites (if required), equipment, student manipulation, provision of space and essentials such as food and water (if held for long periods). Demonstrations of invasive procedures in upper level techniques courses require instructors to be sensitive to animal needs and student concerns. Euthanatization techniques should be in accordance with the American Veterinary Medical Association's recommendations for approved methods of euthanasia (15). Instructors should be familiar with state of the art methodology and have demonstrated skill in performing the technique before being allowed to teach students.

Finally, dedication to exercising the 3 R's (reduction, refinement and replacement) when working with potentially painful procedures can serve as appropriate guidance for agricultural teaching and research. All teaching and research protocols should be submitted and reviewed by the Institutional Animal Care and Use Committee (IACUC).

### **Biomedical Research and Teaching**

Farm animals have made valuable contributions as models in biomedical research (4). Organ transplants, pharmacokinetics, vaccine efficacy, etc. are just a few examples of how farm animals have been used. Special concerns arise when animals who are not customarily bred and raised in laboratory settings, are used for experimental manipulations under such conditions. Flooring, housing, isolation, handling and specialized equipment are all concerns. Experimental manipulations may require extensive contact with the animal for long periods of time, therefore, standard field equipment, traditionally used in agricultural practice for short term restraint purposes, are not practical in many laboratory settings (11). Frequent handling of the animal and familiarization with equipment and routines may be necessary to alleviate distress in laboratory settings. Surgical facilities (especially for large species such as cattle and horses), proper use of analgesia and anesthetics, and pre- and post surgical care are of utmost concern.

Like agricultural teaching, similar concerns can be echoed regarding the use of farm animals in biomedical teaching. Appropriateness and goals of the exercise, skills of the instructor, techniques used, facilities, etc. should be considered. However, in biomedical teaching it is more likely that the animal will be subject to greater manipulations and invasiveness. The 3 R's are expected to be considered in teaching protocols that are potentially painful. Consideration should be given to reducing the number of animals used, looking for alternative teaching technologies and using the most appropriate techniques and equipment for the intended purpose.

Compliance standards under the AWA and/or Public Health Service (PHS) policy must be met for farm animals used in biomedical activities. All protocols must be reviewed by the IACUC.

### **Assessing Farm Animal Well-Being**

Assessing the well-being of farm animals requires that adequate measures have been identified, agreed upon and are quantifiable. In agricultural settings, farm animal well-being has traditionally been assessed by productivity (e.g. growth, weight gain, feed intake, etc.), various health parameters (e.g. disease incidence), a limited number of physiological measures (e.g. cortisol), and animal behavior (e.g. stereotypies, vacuum behaviors). The science of animal welfare is still in its infancy and current investigations are revealing the complexities of well-being assessment. Researchers, although diverse in their proposals of best measures, are in general agreement that a multi-disciplinary approach is needed to assess and define animal welfare in order to understand, alleviate and prevent suffering (13). The concept of animal suffering is controversial (3). Duncan (2) suggests that welfare is determined primarily by how an animal "feels." To suffer, animals must 1) be sentient, and 2) have the ability to be aware of their suffering. Research into cognition,



perception, motivation and the emotional states of animals can provide insight into welfare problems. Others, however, suggest that feelings are too subjective to provide reliable information and that more objective measures based on biological functioning, such as a pre-pathological state (8,10) would be more accurate.

While welfare assessment is very much in debate, reasonable observations can be made to help assess welfare in research and teaching settings. It is reasonable to assume that animal well-being is of a physiological and psychological nature, and that both need to be monitored to the best of our abilities. Aside from the considerations previously stated, careful observations of the animals and of human-animal interactions can provide helpful feed-back. Depression, anorexia, injury, aggressiveness, self-mutilation, sickness and fear responses can be indications that the animal's psychological and/or physiological well-being is impaired. Thorough knowledge of protocols will assist in determining whether such manifestations are expected (e.g. disease research) and addressed, or unexpected and in need of attention, or worse, symptomatic of neglect and poor conduct. Animal caretakers, instructors and researchers all need to develop a keen eye for their animals and address problems in a timely manner.

### **Public Accountability**

During the last twenty years, public concern about the use of animals for experimental and educational purposes has focused on the biomedical community. Federal legislation such as the Animal Welfare Act (AWA) provided impetus behind institutional accountability for the care and use of common laboratory species.

Agricultural animals used in biomedical research are covered by the AWA, at this time, but with no specific standards for their care and use. If used experimentally for the purpose of improving food or fiber production they are exempted from the AWA regulation.

The Public Health Service (PHS) policy sets standards of care for all warm-blooded vertebrates used in PHS supported work. General standards of care for common species of livestock are outlined in the National Institutes of Health (NIH) *Guide for the Care and Use of Laboratory Animals*. Although appropriate for the care of livestock under the experimental settings of biomedicine, the NIH *Guide* falls short of addressing the unique attributes of agricultural production research (1).

Although general concerns about the well-being of farm animals used in either biomedicine or agriculture can be thought to parallel one another, differences do exist in the goals of agricultural and biomedical research and teaching that require guidelines and standards to maximize welfare to differ (12). Agricultural research must have the ability to use its current industry practices as a control in order to address problems in either a basic or applied sense. The ultimate goal is the production of a food product and practices that can be applied in the field. Although application of the 3 R's has been advocated in agricultural teaching and research, there are limits. Replacement of animals is often not an option and may have limited use in teaching or research protocols. For example, when attempting to answer specific questions concerning animal productivity, no other model will be acceptable.

In biomedical research, farm animals are generally used as models for human systems or conditions, the production or testing of products (pharmaceutical, etc.). There tends to be greater experimental manipulation of the animal in biomedical procedures and housing and handling requirements are generally more intensive with rigid standards for laboratory upkeep. The experimental criteria for the use of these animals will vary.



In the mid-1980's a consortium of animal scientists, members of the government and veterinary community, etc., cooperated to develop the *Guide for the Care and Use of Agricultural Animals in Agricultural Research and Teaching*. The *Ag Guide*, as it is presently referred to, is meant to provide institutional accountability, responsibility, and compliance guidelines for farm animals used in agricultural teaching and research. Prior to the publication of the *Ag Guide* there was no vehicle by which welfare concerns could be formally addressed, nor uniform guidelines that agricultural institutions could refer to. Presently the *Ag Guide* has been adopted by a majority of agricultural institutions for setting policy on institutional animal care and use (Mench, personal communication) and the American Association for Accreditation of Laboratory Animal Care has adopted the *Ag Guide* (specie care and husbandry sections) for accreditation of farm animal research facilities.

Maintaining the welfare of similar animals for different purposes in contrasting environments poses a problem with consistent application of guidelines for their care and use. Hence, the potential utilization of three documents (AWA, *NIH Guide* and *Ag Guide*) to ensure their welfare. IACUC's should be well acquainted with all three documents to know under which conditions each of these documents should be applied.

## Conclusions

In closing, I wish to reflect on the idea that no issues would exist if it were not for human concern and commitment to animal welfare. Laws, standards and guidelines are ways in which the research and teaching community can be held accountable to the public for their actions. Animal protection groups frequently seek to strengthen and provide increased oversight of research activities in an attempt to represent the interests of the animal being used. Whereas, the biomedical and agricultural community seek to reach a compromise between human and animal interests that will provide societal benefits yet fulfill expectations regarding animal care and use. I venture to say that most issues concerning the care and use of animals in research and teaching are propelled by the dynamic exchanges between protectors and users of animals. Each of which have made contributions to enhancing farm animal welfare.

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# Recognition of Pain in Farm Animals

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The study of pain in laboratory animals through the past 40 years has presented us with a progressive development in our understanding of the means by which noxious stimuli elicit neural activity, and the neural pathways through which this activity reaches and terminates within the brain. At the same time, we have experienced a growth in our intellectual and philosophical consideration of pain in animals, and have become more concerned about the role of pain in production of stress and discomfort in all laboratory animals (6).

The inclusion of farm animals into these considerations has been a fairly recent but not unforeseen development. The explanation for delay in the inclusion of farm animals fully into the arena of research, teaching and testing animals likely resides in the desire to isolate these practices from production practices. There are many common practices in production of animal meat and fiber that would not be considered acceptable under the current guidelines for care and use of laboratory animals. It is necessary, however, that these practices be considered on their own merit in an attempt to apply current federal guidelines to the use of farm animals in research, teaching and testing.

It is my philosophy (and one that I think should be emphasized within our Institutional Animal Care and Use Committee (IACUC) membership) that there is a basic level of humaneness that must be applied to all species used in research, teaching and testing. I feel that this level also applies to production practices. Beyond this level, other considerations of pain perception and humane treatment is determined by the protocol applied to the animal. In the following discussion, I wish to raise some consideration of factors influencing the nature of pain sensations in animals in general, and particularly in farm animals. I hope that these considerations may be helpful in establishing the characteristics of that basic level of humaneness as it is applied to a specific research, teaching or testing protocol.

Pain has been recognized through the centuries as a word that describes a wide range of unpleasant experiences in humans (8). It has continually been recognized that it is difficult for humans to share what they have felt as a pain sensation, and to describe this experience to their own satisfaction. Realizing that the concept of pain perception is derived entirely from our human experience, and that we by necessity have extrapolated this concept to animals, leaves one with little wonder that there are difficulties in interpreting sensory and meaning phenomena within this extrapolation.

There was a time, not so long ago, when pain scientists were relatively comfortable with their understanding of the anatomic, physiologic and behavioral aspects of pain perception in animals (3). Specific "pain pathways" had been identified within the spinal cord and brain that underlie pain perception and the behavior it elicits. These were taught to veterinary medical students, to be memorized as the anatomic basis for pain perception in animals. Elaborate behavioral studies were conducted to confirm that these pathways did indeed serve as the anatomic substratum for pain perception (3). It was generally considered that wherever pain was to be evoked in an animal, anesthesia and/or analgesics would be applied. These were the days before there was a great deal of



attention given to the need for extensive considerations of pain induction by the methods applied in the use of animals in research, teaching and testing.

It was clearly recognized that there were anatomic substratum differences between non-primate laboratory animals and humans. These anatomic substratum differences appeared to represent degrees of neurologic differentiation. They were interpreted to represent differences in the specificity of central nervous system structures in the processing of neural information concerned with pain perception (4). There could not, however, be allowed the consideration that there might be a difference between the actual sensation experienced in man and animals. The difficulty that these anatomic differences produced was that the only pain perception that we, as investigators, or oversight persons of IACUC responsibility, have ever experienced is our own pain. If we did not perceive pain, if this pain was not unpleasant to us, and if this pain did not induce suffering and distress in us, we would not be considering whether or not it occurs in laboratory animals.

It is necessary to assume that animals perceive pain with all its variations in intensity, sharpness, dullness, localization, or diffuseness, exactly as it is perceived by human beings. If this premise does not hold, then it is impossible to study pain in animals, because there would be no standard against which it could be measured. It was, and still must be accepted, therefore, that if a given stimulus evoked a pain sensation, emotional and escape reaction in a human, and if the application of that stimulus will evoke a similar emotional or escape reaction in an animal, that stimulus produces pain perception in the animal. It must be emphasized that it must be considered that pain perception does not differ from that perceived by a human being in the same situation.

If, however, we are to use the human as the standard, it is necessary that we clearly characterize the standard before it is applied. There are some characteristics of pain perception that are well known through everyday experience in humans that are basic to our ability to determine, quantify and characterize pain perception in animals. I do not think that we can abandon the anthropomorphic basis of evaluating pain in animals. This is the only basis we have. I do feel, however, that it is necessary that we apply this basis from a realistic point of view. The emphasis that I would like to make is that there are some differences in our lives from those of farm animals that do make a difference in the significance of pain perception.

The difference that I would like to emphasize is our anticipation of pain and the impact of this anticipation on our perception. We learn, through personal experience, or the experience of others to anticipate pain in certain circumstances. Although animals may learn through experience, they are not generally preconditioned, to the degree experienced by humans, by the experience of others. Whether or not pain perception would normally be elicited by a given circumstance, if we think we will perceive pain then when the stimulus is applied, we *will* perceive pain. Some of you may have been in the old U. S. Marine Corp, (before the 60's), or have joined a fraternity in college in which hazing was common. The experience with the blow torch, hot iron and application of ice, that you were certain burned a hole in your skin, typifies this conditioning. This preconditioning often makes it difficult to evaluate pain perception in humans. A stimulus that is apparently innocuous in one human subject may induce an excruciating painful experience in another.

A good example to illustrate the effect of preconditioning, and the difference it makes in suffering or distress, is the comparison of a human who has undergone laparotomy, and intra-abdominal surgery, compared to a laboratory animal (rat, dog, cat or farm animal) undergoing that same surgery. The human, through anticipation, anguish, and concern for the pain to come, often suffers the pain even before the act of surgery occurs. I have never experienced an animal, except in cases where multiple serial surgeries are performed, to demonstrate any degree of anticipation to surgery. After the surgery, the typical animal is on its feet, eating, running, grazing, whatever is natural for it do. The human, on the other hand, is slow to recover, complains of much pain, and takes days to weeks to recover. This difference, not only in pain, but also the distress produced by it,



is an important consideration in the evaluation of pain perception in farm animals from a strictly anthropomorphic point of view. It is clear that in these circumstances, we depart from the strict anthropomorphic interpretation of pain and distress in animals, but let the animals "speak" for themselves through their behavior.

The sensations that are described as pain in humans, and assumed in animals (due to their anthropomorphic responses to situations in which these sensations are generated), represent a wide spectrum. We can quickly recognize that there are differences in the sensation produced by a pin prick or a burn, and one produced by neuralgia. These not only represent differences in type of sensation evoked, but also represent different stimulus modes through which the sensation is induced.

At one end of the pain sensation spectrum are the well known protective sensations. These are usually evoked by "applied stimuli" such as burns, needle sticks, electric shock or other stimuli that are noxious to cells and tissues. In farm animals used in research, teaching and testing, this "induced pain" represents the majority of sensations referred to as pain. Induced pain initiates alarm, withdrawal, escape, or attack responses that are often accompanied by vocalization in farm animals. In humans experiencing induced pain, there is a good correlation between the afferent neural activity induced in peripheral nerve axons and the intensity of subjectively perceived pain (8). The intensity of induced pain in farm animals, that is acceptable in a research, teaching or testing protocol, is difficult for investigators and IACUC members to discern. The presence of pain associated reflexes, along with voluntary, or "willed" behavior usually serves as the basis for judging whether or not a pain perception takes place. It is generally accepted that there is a level of pain perception that is acceptable. This allows the consideration that in trained hands, needle punctures for the normal clinical collection of blood produces an acceptable level of pain or discomfort. For each protocol, that goes beyond this level, the investigator and members of IACUC must use their judgement concerning the intensity of pain induced.

At the other end of the spectrum are non-protective pain sensation syndromes produced by organic or patho-physiological mechanisms. This type of pain sensation is generally the consequence of naturally occurring, or experimentally induced peripheral or central neuropathies (1). It can reasonably be referred to therefore, as "neuropathic" pain. It is the sort of pain that is experienced in neuralgia, so familiar to humans (11). Such neuralgias may be induced in animals by disease processes, or by experimental processes (7). Polyneuropathies, diabetes, toxin or viral induced, can result in the production of intense pain perception in humans, and must be considered to do so in farm animals as well. It is necessary that investigators and IACUC members be cognizant of this type of pain induction, and its significance in producing distress that may interfere with the well being of the animal and the outcome of the research (5). A portion of the campus educational program provided to animal research personnel should include discussion of the possibility of neuropathic pain induced by specific types of experimental protocols.

Between the two extremes of "induced" pain and "neuropathic" pain is pain that is associated with inflammation. This "inflammatory" pain is distinctly different from the two extremes, in that it is induced by mechanisms of tissue response to injury, rather than an external stimulus that would be regularly considered to induce pain perception (9, 10). The pain associated with inflammation usually requires some additional stimulus for initiation, but this stimulus need not be noxious (which implies damage, or potential damage to tissues). Even the slight movement, or lightest tactile stimulation may initiate pain perception in the presence of inflammation.

Recognition and prevention of pain induced distress in farm animals, as in other species, is aided by a knowledge of the neuro-physiological mechanisms underlying pain sensation. This knowledge is particularly necessary to those directly responsible for use of animals in research, teaching or testing, in order that they may discern whether or not, toxins, microbiological agents or

drugs used in their protocols may mask or prevent a response to pain. These animals may demonstrate a number of distress responses that are not clearly discerned as due to pain induction.

Although it is necessary that the judgement of the distress producing capability of pain sensation be anthropomorphically based, those who use farm animals as laboratory animals, and IACUC members must also be aware of protocols that are likely to induce pain in circumstances in which it would not ordinarily be expected in humans. It is equally as important that those judging research protocols on the basis of animal responses, be aware of normal animal behavior. In most farm animals, unsocialized with humans, even the slightest stimulus, whether it be noxious or not, may induce vocalization, alarm, withdrawal, escape, or attack responses that could easily be ascertained as induced by pain or discomfort. Recognition of pain perception in farm animals, as in other species, requires a thorough knowledge of the normal animal of that species. Chronic pain perception, or chronic distress from any cause generally results in decreased appetite, motility, milk, egg or meat production in farm animals.

There is no list of signs that infallibly indicate that pain is being perceived in any given farm species. There are some characteristics of individual animals within a farm species, or often within a species as a whole, that are helpful in making this determination and of estimating the degree of discomfort that is present. If there is any doubt, however, concerning whether or not an animal is experiencing undue, or unacceptable levels of pain, one should consult a veterinarian or animal husbandryman who is familiar with the species in question. Usually the animal care personnel are the first to know when an animal is distressed by disease or a pain inducing process. They should be an integral part of this evaluation.

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# Large Animal Anesthesia

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This discussion reviews some of the common anesthesia problems when dealing with the large animal species used in research. This includes cattle, sheep, goats and swine.

## Neonatal Anesthesia

Frequently, research projects require general anesthesia for neonates of farm animal species. The neonate has several significant physiological differences from the adult animal that affects anesthesia. These differences include:

- The blood brain barrier is poorly developed because the junctions between endothelial cells and the choroid plexus are wider than in the older animal. As a result, induction of anesthesia may be quicker and requires less drug than in the adult animal(1).
- Hypothermia. Neonates have a greater body surface:body weight ratio (2). As a result, they lose heat more rapidly than adult animals. With hypothermia, drug metabolism is retarded and the neonate may be slow to recover, especially from injectable anesthetics that depend primarily on metabolism for complete recovery.
- Hypoproteinemia. Plasma protein levels, particularly albumin levels, are lower in the neonate than in the adult. This means that neonates are more likely to develop pulmonary edema from intravenous fluid therapy (3). Also many anesthetic drugs are protein bound. Therefore, smaller doses of anesthetics may be required (particularly barbiturates) than in adults. It is the nonbound anesthetic that crosses the blood brain barrier (4).
- Low body fat content. Fat represents a storage depot for anesthetic drugs. In the case of neonates, the lack of body fat means that redistribution of anesthetic drugs will be delayed and recovery will be slow due to prolonged plasma levels (5).

Hepatic function and hypoglycemia. In general, the clearance of drugs by the liver is less than in the adult. Microsomal enzyme development is incomplete resulting in the delayed clearance of drugs (6). Neonates also have poor glycogen stores, consequently, hypoglycemia can readily occur in the stressed neonate (2).

## Anesthetic Techniques for Neonates

Because of the various alterations of normal drug metabolism listed above, it is often preferable to use anesthetic drugs that are minimally metabolized, namely, the inhalant anesthetics.

Because neonatal animals are more readily restrained and induction is quicker than in the adult, mask induction is easily accomplished. A mask is loosely applied to the nose and mouth and oxygen only is first administered. This reduces anxiety about the mask and also increases the arterial



oxygen of the patient. After at least one minute of oxygen only by mask, the anesthetic gas is delivered. Some anesthesiologists prefer low concentration of anesthetics at first while others recommend high concentrations immediately. Nitrous oxide can also be used to speed the induction time. If the patient is struggling severely, the quicker one can induce anesthesia the better. After the patient is anesthetized via the mask, the animal should be intubated and the endotracheal tube cuff inflated.

Another method of inducing anesthesia is nasotracheal intubation. This method works well in foals (7) and calves (8). In this, endotracheal intubation is performed with the animal awake, utilizing the nasal route. The neonate tolerates the tube in the nose and trachea amazingly well. The tube, with cuff inflated, can then be attached to the anesthetic machine and anesthetic delivered as described in the previous paragraph. The tube can be left in the nasal passage or the animal can be reintubated orally.

In summary, the neonate can readily be anesthetically managed with gas anesthesia only. Because neonates can be easily restrained and little metabolism of inhalant anesthetics occurs, the inhalants are an excellent choice for neonates. The recovery from inhalants is smooth and rapid which means the neonate can be returned to its normal environment shortly after the anesthetic procedure.

## **Ruminant Anesthesia Problems**

### ***Regurgitation***

Ruminants are prone to regurgitate and aspirate the rumen contents with anesthesia. Regurgitation is a result of several factors. Anesthetics relax the pharyngeal-esophageal sphincter and the reticulo- esophageal sphincter. Anesthetics also depress the swallowing reflex, thereby reducing the animals ability to protect its airway from any regurgitated material. When the ruminant becomes recumbent, pressure is applied to the rumen. This increase in rumen pressure with sphincter relaxation results in regurgitation.

To reduce the incidence of regurgitation and aspiration, fasting prior to elective anesthetic procedures is indicated. The guidelines for fasting prior to anesthesia are as follows:

- Adult cattle: withhold food for 24-36 hours and water for 12-24 hours prior to anesthesia
- Small ruminants: withhold food for 12-24 hours and water for 0-12 hours prior to anesthesia
- Ruminants less than 1 month of age are not fasted prior to anesthesia.

In addition to fasting, intubation is highly recommended. Use of a properly inflated, cuffed endotracheal tube will protect the lower airways from regurgitation.

### ***Bloat***

Anesthesia eliminates the ability of the animal to eructate. Also during anesthesia, rumen motility is reduced. These two factors lead to gas formation that, if excessive, will result in pressure on the diaphragm and a decrease in lung volume. Ventilation perfusion (V/Q) mismatching occurs during anesthesia in large animals because of gravity and blood flow changes due to decreased cardiac output (9). V/Q mismatching is accentuated by bloat and results in a further decrease in oxygenation. Proper fasting as discussed above will diminish the incidence and severity of bloat during anesthesia.

## ***Injury***

Induction and recovery injuries such as fractures can occur even with the best of facilities but they should never occur because of poor facilities. Adequate restraint and trained personnel are essential for successful inductions of general anesthesia of large animals.

Nerve paralysis is usually due to prolonged anesthesia, with inadequate padding or positioning. Post-operative myositis may also be due to prolonged down time with inadequate padding (10). However, myositis can be due to poor perfusion of muscle during anesthesia. This can be attributed to failure to maintain adequate cardiac output and sufficient blood pressure for adequate muscle perfusion.

## **Preanesthetic Sedatives**

### ***Xylazine***

Xylazine, an  $\alpha_2$  adrenergic agonist, can be used as a sedative in low dosage. Ruminants are very sensitive to xylazine. The dose in ruminants is approximately one-tenth that used in the horse. However, xylazine is not approved for food producing animals.

The following dosage guidelines are for healthy adult animals not receiving any other preanesthetic drugs.

Xylazine Doses:	Cattle	Sheep & Goats
Sedation	0.02 mg/Kg IV, 0.05 mg/Kg IM	0.1-0.2 mg/Kg IM
Recumbency, heavy sedation	0.11 mg/Kg IV, 0.22 mg/Kg IM	0.22-0.66 mg/Kg IM

### ***Detomidine***

Detomidine is an  $\alpha_2$  adrenergic agonist that has similar characteristics to xylazine. It is, however, much more potent. It is approved for use in the horse but not in food producing animals. The suggested dosage for cattle is 20-80  $\mu$ g/Kg IM (11).

## **Side Effects of Alpha 2 Adrenergic Agonists**

The most common life threatening side effect of  $\alpha_2$  adrenergic agonists in ruminants is bloat. Rarely is this a significant problem if the animal has been properly fasted. Treatment, in addition to sternal positioning and stomach tube passage, could include the use of an  $\alpha_2$  adrenergic antagonist.

Excessive salivation frequently occurs following the use of  $\alpha_2$  adrenergic agonists. The use of atropine is not very effective and of very short duration. Treatment of excessive salivation consists of preventing its tracheal aspiration by keeping the nose and mouth of the animal lower than the pharynx.

Bradycardia occurs with  $\alpha_2$  adrenergic agonists. Treatment with atropine is rarely necessary but will correct the bradycardia. For cattle exhibiting bradycardia (Heart Rate <30) due to  $\alpha_2$

agonists, the initial intravenous dose of atropine is approximately 0.02 mg/Kg. If no response is seen the dose should be repeated.

## **Alpha 2 Adrenergic Antagonists**

These drugs are used to reverse the effects of  $\alpha_2$  adrenergic agonists. Reversal is usually rapid and complete, however, results in ruminants with yohimbine have been variable (13) while tolazoline and yohimbine have produced variable results in horses (14). Idazoxan and atipamezole are very specific  $\alpha_2$  adrenergic antagonists but are not readily available at present.

## **Anesthetic Combinations for Sheep, Goats, and Cattle**

The following methods of producing anesthesia are for procedures usually less than forty-five minutes or for induction/intubation of gas anesthesia. Since most anesthetics are not approved for use in food producing animals, these recommendations are for animals not entering the food chain.

### **Sheep and Goats**

#### ***Xylazine/Ketamine***

In this combination the two drugs are given according to the dose listed:

Xylazine	0.22 mg/Kg IM
Ketamine	11 mg/Kg IM

The amount of gas anesthesia during the first 15-20 minutes of the procedure would be minimal. As the xylazine: ketamine combination is eliminated, gas concentrations will need to be increased.

### **Cattle**

#### ***Thiopental/Guaifenesin***

This combination is a very reliable method of producing general anesthesia with good muscle relaxation. Guaifenesin is a central acting muscle relaxant that can be purchased in powder form or solution. The barbiturate, thiopental, is added to the guaifenesin solution.

The dosage for healthy cattle is as follows:

Thiopental	6.6 mg/Kg IV (5 Gm max dose)
Guaifenesin	100 mg/Kg IV (50 GM max dose)

Guaifenesin is usually prepared in a 5 or 10% solution with sterile water, saline or 5% dextrose. If the 5% solution is used a large bore catheter (10-12 ga.) is required for rapid administration to provide a smooth induction of adult cattle.

## **Anesthetic Methods for Swine**

Adult swine can be very difficult anesthetic patients. Both intravenous and intramuscular routes have been used for anesthetic procedures of short duration or for induction of gas anesthesia.

Intravenous thiopental or thiamylal at a dose of 9-11 mg/Kg is used for procedures of 5-10 minutes duration and for tracheal intubation. A combination of xylazine/Telazol® (teletamine-

zolazepam) can be used via the intramuscular route. The dosage is xylazine (1.1 mg/Kg) and Telazol (3 mg/Kg) given intramuscularly.

## **Inhalation Anesthesia**

As research surgical procedures have become more sophisticated the need for quality anesthesia of long duration has developed, the use of inhalation anesthesia has increased.

Some of the reasons why gas anesthesia is superior to injectable techniques without respiratory support include:

- Provides a patent airway. Gas anesthesia usually utilizes an endotracheal tube. This insures an open airway and saves valuable time in an emergency when respiratory control is required.
- Improves oxygenation. Because oxygen is used as the carrier gas for inhalant anesthetics, arterial oxygen tension is much higher than in animals breathing air. This is of particular importance to large animals because of low oxygen tension during anesthesia.
- Facilitates control of ventilation. By using positive pressure ventilation, arterial carbon dioxide levels can be maintained near normal preventing cardiac arrhythmias that may develop with a respiratory acidemia.
- Control of the depth of anesthesia. During surgery the analgesic requirements may vary. Changes in the depth of anesthesia can be quickly achieved. If emergencies arise, the administration of inhalants can be stopped immediately and the system flushed with oxygen to hasten recovery.
- Smooth and rapid recovery. Because almost all inhalant anesthetic is eliminated via the respiratory system, recovery is relatively quick and with minimal excitement. Injectable anesthetic techniques, however, depend upon metabolism for elimination of the agent.

## **Inhalation Anesthetic Agents**

• There are two primary inhalation agents, halothane and isoflurane. Both of these agents require the use of out of circle vaporizers. Nitrous oxide can be used with both agents to speed induction and to reduce the amount of primary agent required to maintain anesthesia. The use of nitrous oxide, however, is not recommended for ruminants because of the risk of arterial hypoxemia and bloat.

### ***Halothane***

Halothane has a MAC (minimum alveolar concentration) of approximately 0.9% for most species. The MAC value is a measure of a gas anesthetic's potency. By knowing the MAC value one can estimate the maintenance level of anesthetic (vaporizer setting) required for surgical anesthesia. The vaporizer setting is in the range of 1.5-2 times the MAC value. For halothane the vaporizer setting is approximately 1.5-2%. The vaporizer setting may be reduced by preanesthetic and induction agents. Halothane can be used for mask inductions of neonates since it produces a relatively quick induction with minimal excitement.

The effect of halothane on the cardiovascular system has been studied extensively (15,16) Halothane is a very useful and relatively inexpensive inhalant anesthetic and will continue to be a widely used agent in all species.



## *Isoflurane*

Isoflurane has been available since the early 1980's. The advantages versus halothane include a quicker induction and recovery with less cardiovascular depression. The incidence of dysrhythmias during isoflurane anesthesia is substantially reduced when compared to other agents (15,16). Isoflurane is relatively expensive to use when compared to halothane.

Isoflurane has a MAC value of approximately 1.3%. This translates to a maintenance level (vaporizer setting) of 2-3%. Malignant hyperthermia, previously reported in swine exposed to halothane, may also occur with exposure to isoflurane (17).

## **Epidural $\alpha_2$ Adrenergic Agonists and Opioids**

Recently there has been considerable interest in the use of epidural anesthesia both for providing surgical anesthesia and for post operative analgesia. Xylazine has been the primary drug utilized for surgical anesthesia. Xylazine has been administered epidurally, primarily at the coccygeal<sup>1</sup> - coccygeal<sub>2</sub> space, for both horses (18) and cattle (19). The onset of anesthesia is slower than that seen with lidocaine but is longer in duration. Also in the bovine, the analgesia advances forward to the flank area with the patient remaining in the standing position.

Opioids have primarily been used for post operative analgesia. Epidural morphine in the dog has been used to provide post operative analgesia lasting up to 24 hours. The amount required is much less than that given intramuscularly for analgesia and does not interfere with motor function or produce depression of the cardiovascular system.<sup>20</sup> The use of epidural opioids in food animal species requires further investigation before any recommendations can be made.

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# Post-operative Care And Analgesia of Farm Animals Used in Biomedical Research

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## Introduction

Farm animals are being used with increased frequency in research facilities. As biomedical researchers and investigators, we must recognize and accommodate their unique husbandry needs. These farm animals should be housed in areas designed specifically for them. Unfortunately, it may not be advisable to put pigs or goats in a facility's largest dog pens. These animals will probably be less domesticated than the typical research cat or dog, and the "human contact" factor may not be as essential to their well being. However, their needs should be considered as we prepare to house them for extended periods of time. The environment that the animals encounter, beginning with their initial entrance into the facility, can contribute to a smooth operative and post-operative period. They should be housed in the least-stressful environment possible. Food and water intake, as well as social behavior, should be monitored as an indication of overall well being. More research is needed to develop analgesics that address some of the challenges these animals present during the post-operative period. Farm animals used in biomedical research would benefit from analgesics with longer duration times, increased routes of administration and shelf-life, reduced addictive potential, and wider margins of safety. As we increase our usage of farm animals in invasive surgical procedures, we are obligated to circumvent post-operative pain and other stressors resulting from our experimentation.

## Pain Perception and Analgesics

As ethology research increases, hopefully our knowledge of the expression of animal pain will increase proportionally. Being familiar with the normal behavior is imperative in assessing abnormal activity and temperament in farm animals. Parameters for "normal" behavior vary not only from one species to another, but also from one individual animal to another. It may prove to be a very expensive endeavor, both in time and money, to engage in any research protocol without first thoroughly familiarizing yourself with the normal activity of your animal model. Close communication between animal caretakers and the researchers works toward the best interest of the animal in the post-operative period. An astute caretaker's knowledge of the normal behavior for that particular age, sex, species, and individual is crucial in determining when animals are experiencing unacceptable levels of pain.

One of the best clinical assessments in distinguishing normal from abnormal behavior is the feeding pattern. Many species of farm animals experiencing pain and distress do not eat normally. However, this does not mean that any animal that seeks food post-operatively does not need pain management. When animals are housed in a group, it would be helpful to remove the post-surgical cases for daily weight checks. A reduction of food intake will also be reflected in fecal and urine output. Too, the animal that separates itself from the rest of the animals with which it is housed may need additional attention. Other signs of discomfort may be an alteration in an animal's gait or a constant changing of position. Also, some species of farm animals (especially goats) will increase their vocalizations when in pain. Pigs are notorious for becoming either aggressive or seeking



solitude when they are uncomfortable. Sheep seem to be unique in their ability to tolerate high levels of pain with only minor changes in their normal behavior. The need for researchers to learn the normal behavior of their particular animal model is easily understood.

There is a general consensus that animals perceive pain. However, as researchers we have been slow to respond to this awareness, especially when farm animals are used in biomedical research. As farm animals become increasingly popular in research, it is not only appropriate, but also an obligation for researchers to familiarize themselves with both the obvious and the more subtle signs of pain and discomfort in these large animal species.

We should assume that any procedure that would cause pain in humans will also cause comparable discomfort in farm animals. Invasive procedures causing tissue injury should be expected to result in varying degrees of post-operative pain. When this is anticipated, a plan should be in force to administer appropriate tranquilizers and analgesics post-operatively. The goal is not directed toward giving relief so much as it is toward *circumventing* pain by designing a protocol which includes adequate analgesics given prior to the onset of severe discomfort.

As we decide on appropriate analgesics, the surgical procedure must be considered. Certain surgical sites are likely to present a greater pain management challenge than others. Extensive surgical procedures involving the areas of the cervical spine, sternal approaches to the thorax, the head, eye, ear, mouth, rectal area and bones will all generally result in moderate to high degrees of pain post operatively. Since this sensitivity has been documented in other species, we should investigate which analgesics would be most appropriate for those experiments requiring surgery in these areas.

The proper analgesic selection has much to do with the particular animal model that is being used. Some research has been performed that compares differences among common domestic farm animals and their ability to utilize various analgesics. There are species differences that influence the deposition of analgesic drugs. These differences, many of which are anatomical, will affect the selection and route of administration for various analgesic drugs. The digestive tracts of various domestic species reflect a difference in the drug deposition. For example, swine have simple stomachs with a spiral colon. It has been reported that this feature does not greatly influence drug deposition. Yet horses, being herbivorous, rarely have an empty stomach, and there follows a reduced opportunity for the drug to be absorbed. Cows and other ruminants have large acidic environments in their digestive tracts from which many drugs are not easily absorbed. Also, many drugs are destroyed by the enzymes produced by the ruminal flora. These factors should be remembered as researchers decide on their armament of pain medicines.

### Specific Analgesics

Opioid agonists (morphine, meperidine, oxymorphone, and fentanyl) and agonist-antagonists (pentazocine, butorphanol, nalbuphine, and buprenorphine) are two groups of effective analgesics. Opioid agonists probably have the best reputation for providing potent analgesia. When administered in analgesic dosages and given intramuscularly or subcutaneously, they are unlikely to cause detrimental side effects. Unfortunately, in farm animals the use of morphine and other opiates is known to cause excitement. Therefore, when opiates are used for analgesic purposes in farm animals, they are used in conjunction with other drugs.

Analgesics work best when their use is initiated to *prevent* post-operative pain. Low doses of analgesics given prior to full recovery mean that fewer analgesics will be necessary and that any pain will be more readily managed.



Opioid agonist-antagonists have some advantages over opioid agonist. They have limited abuse potential and are not strictly controlled. They do not produce the profound analgesic response that characterize the opiates; however, they can be very helpful in pain management. These drugs also have a "ceiling effect," and depending on the given situation, this may or may not be an advantage. Increasing the dosage of butorphanol, for example, above the optimal dose does not increase the analgesic effects or incite respiratory depression. The advantage of this is that the respiratory system is spared from further depression. However, the analgesic effects are also limited by this same "ceiling." Another advantage of these opioid-antagonists is that they can be used to antagonize opioid agonist.

Buprenorphine appears to be one of the longer acting agonist-antagonists. It has the advantage of being able to be administered by various routes (IV, IM, SC, and IP). However, the most encouraging aspect about this drug is that dose intervals are up to 12 hours in pigs, and 4-6 hours in sheep and goats.

Nonsteroidal anti-inflammatory drugs, although commonly overlooked, can be very helpful in the management and treatment of post-operative pain. Many of these drugs (aspirin, ibuprofen and phenylbutazone) are excellent anti-inflammatory, antipyretic and analgesic agents. The disadvantage is that they modify the release of arachidonic acid, and this may interfere with experimental studies. They are not the potent analgesics that the opiates are.

Meperidine, a commonly used opioid agonist, has been found to have an undeserving reputation as an analgesic drug in farm animals. The literature is now showing that this drug has a half-life of less than one hour, making its use in farm animals less than practical. Likewise, pentazocine has been shown to have very rapid elimination from farm animal species.

## Suggested Practical Analgesics for Farm Animals Used in Biomedical Sciences

### Ruminants

aspirin	50-100 (mg/kg) PO	12 hours duration
phenylbutazone	6 (mg/kg) IV,IM,PO	
buprenorphine	.005 (mg/kg)	4-6 hours duration

### Pigs

aspirin	10 (mg/kg) PO	
phenylbutazone	2-5 (mg/kg) IV	
buprenorphine	0.1 (mg/kg) IM	12 hours duration

## The Post-operative Period

The recovery period should be viewed as the final stage in the surgical procedure. Some investigators and their staff have underestimated the importance of this stage of the surgical endeavor. There can be no successful surgery with an unsuccessful recovery. Often, mistakes made during the surgical procedure come back to haunt the research staff during the recovery stage. For example, large pigs that were given excessive doses of a barbiturate experience a protracted recovery period.

Post-operative care should be assigned to a particular person on the research team. The recovery of animals used in surgical experimentation should take place in a specific area designed to meet the special needs of animals during the post-operative period.

The post-operative environment should be characterized by a room equipped with subdued lighting. The ambient temperature should be near 27-30 °C for young animals and 35-37 °C for an

adult animal. It is important to monitor the body temperature as well as the environmental temperature. As the animal recovers, it will regain the ability to maintain its own temperature and diminish the need for heating pads, etc. Care must then be taken to insure that the animal does not become over-heated.

The maintenance of a patent airway is important in any recovering animal. An endotracheal tube should remain in position until the animal's swallowing reflex has returned. This dimension has increased importance in certain species, such as the pig, an animal that has a tendency to vomit.

Small ruminants (sheep and goats) should be placed in a sternal position. This position tends to reduce the incidence of overdistention of the rumen and the aspiration of rumenal contents. Repositioning to avoid hypostatic pneumonia is important if the animals are still recovering after 3 to 4 hours.

Animals recovering from surgical procedures should do so in a warm, dry environment. Farm animals should be allowed to recover on fresh bedding, such as straw. Providing a thick, non-skid surface will reduce the incidence of pressure sores and injury as the animal attempts to stand and ambulate.

One of the major problems in providing the ideal recovery room for farm animals is the recurring problem of adequate space. A large-size room is absolutely necessary for large animals as they recover from surgery. This can become a major problem in situations where up to 25 surgeries may be performed on a group of experimental goats or sheep in a single day. These animals need to be placed several feet apart while they recover. Incidents have been recounted wherein adequate space was not provided, and sheep were stacked on top of one another **during** recovery from general anesthesia. An unfortunate scenario developed from one such situation--one of the sheep on the bottom died from suffocation, while many of the others had to be treated for rumenal tympany.

Optimal recovery conditions may be even more important for farm animals used in research than they are for rodents, dogs or cats. The farm animals commonly used in biomedical research (sheep, goats and pigs) are less likely to be amenable to the routine handling required in the case of any post-operative complications. It is in the best interest of the investigator to reduce the need for restraining these animals unless it becomes absolutely necessary. Therefore, maintaining a clean surgical incision and supplying clean bedding may reduce the incidence of having to treat post-operatively. As these animals recover, they are also more likely to be fearful and nervous. A non-skid floor surface in an area with reduced noise and lighting will all encourage a smooth recovery.

A time-interval record-keeping system should be operational in the recovery area. At specific intervals, the heart rate, respiratory rate, temperature, and acid-base status should be monitored on each recovering animal. Such intermittent recording of various vital signs requires a commitment on behalf of the researcher and the nursing staff, helping to magnify the importance of the recovery stage to those individuals keeping records.

## Summary

As researchers plan surgical procedures, post-operative analgesics should be an important consideration. Analgesics must be selected based upon the specific farm animal involved in the experiment. It should be assumed that any invasive surgery, and perhaps some minor surgeries, will require post-operative pain medication. These drugs should be given *prior* to the onset and clinical manifestation of severe pain.

The best attitude to adopt, in order to avoid unexpected events in the recovery room, is one of prevention. By anticipating and preparing for worst-case scenarios, recovery room technicians are forced to mentally rehearse actions to be taken in the case of an emergency. The recovery of farm animals may present a distinct problem because of the large amount of space required for a safe recovery. As researchers routinely make provisions for monitoring animals during the post-operative period, failure to make arrangements for the essential post-operative needs will become increasingly unacceptable. No environment in a research facility can ever be totally free of factors that stress the research animals. However, it is our moral and scientific obligation to reduce, for the entire duration of their stay, the chronic and extreme stressors placed upon the animals entrusted to our care.

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# Agricultural Animal Care Review

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The care and use of agricultural animals at land-grant institutions have received less attention in terms of review procedures than the care and use of conventional "laboratory animals." This is principally because 1) farm-type animals are seldom involved in Public Health Service (PHS) related research and, therefore, may be exempted from institutional assurance statements to those agencies; and 2) farm animals have generally been exempted from Federal regulations. However, with the U.S. Department of Agriculture's (USDA) recent intent to regulate certain categories of agricultural animals based upon the type of usage rather than the species, institutions are wrestling with the appropriate means of oversight.

Farm animal research has traditionally involved production and nutritional studies to enhance the productivity and efficiency for meat, milk, and fiber production. Cattle, swine, sheep, goats, and poultry are commonly researched under commercial-like pastoral or housing conditions. Some research, such as nutrient utilization, reproductive and other physiological studies, and animal health, is conducted under confinement conditions. Surgery is not commonly performed in farm animal research other than routine husbandry practices (i.e., dehorning and castration).

Recently, a consortium of several professional societies developed guidelines for the care of farm animals used in research. The "Consortium for Developing a Guide for the Care and Use of Agricultural Animals in Agricultural Research and Teaching" recommended minimal care standards for housing, handling, nutrition, and space requirements of farm animals. In the absence of Federal guidelines, many universities and USDA laboratories have adopted these guidelines and established formal institutional review procedures. However, several issues still prevail involving the use of agricultural species in research. These issues are:

1. USDA Animal and Plant Health Inspection Service (APHIS) recently redefined the coverage and use of "horses" as a non-agricultural species.
2. Some schools review veterinary research, but have not extended coverage to include animal science departments.
3. Some institutions have one committee that oversees all animal work (regardless of species or the focal point of the research, i.e., biomedical or animal husbandry). Other institutions have established separate, but somewhat parallel, review committees (i.e., a lab animal/biomedical research review and an agricultural/farm productivity committee).

Let us look at the current status and the broader implications of these few situations.

A determination of whether to add this type of research oversight to a pre-existing Institutional Animal Care and Use Committee (IACUC) or to form a separate farm animal care and use committee must be made. Institutions with a strong agricultural component must weigh the pros and cons of each approach. The following considerations support adding these duties to an existing IACUC:



1. **Utilizes Experienced IACUC.** Most IACUC's now have considerable expertise in dealing with existing laws and policies governing animal welfare. Members have learned how to conduct protocol reviews, inspect facilities and programs, conduct investigations of purported misuse of animals, and handle all the required paperwork. The committee is properly constituted in terms of membership, includes an outside community member, and, in most instances, has an adequate support staff for the required clerical work.

2. **Provides Uniformity of Reviews.** Having only one committee aids in providing uniformity of protocol reviews. When researchers submit their protocols, they have a better understanding of what is required from them in terms of the paperwork and degree of justification required on the forms. [Note: Should the institution opt for a dual committee approach, it may be possible to use the same animal use protocol form for each committee, thereby reducing the confusion.]

3. **Prevents Duplication of Effort.** Having more than one animal care and use committee, while permissible under the law and the PHS policy, may: (1) create duplication of effort (i.e., may involve visits to the same facility by multiple oversight groups); (2) place an additional burden on the attending veterinarian (who is often required to serve on both committees); and (3) include the risk of a review by the wrong committee.

A review by the wrong committee can be particularly problematic if the farm animal committee was established to deal only with farm animal subjects used for production purposes and did not intend to follow all of the federally mandated requirements of the traditional IACUC's (i.e., semiannual review of programs and facilities, limited use of expedited reviews, issuance of formal reports to the institution official, etc.). In such a situation, the determination of what constitutes agricultural use versus nonagricultural use becomes of paramount importance and can be difficult to determine. For example, one institution might determine that embryo transfer studies are agricultural in nature and are exempt from the new regulations. Another institution, however, might consider that particular procedure as "biomedical" or nonagricultural and would require review by a legally constituted committee. Disease studies involving meat-producing animals (i.e., brucellosis) could easily fall into this "grey zone" and, thus, be routed differently by different institutions.

The real controversy that will ultimately arise is when the USDA inspector reviews the files and makes the determination that studies are not being reviewed in accordance with the Animal Welfare Act because of a difference in interpreting what is agricultural research and what is not. Therefore, if an institution chooses to set up two committees, one for regulated research and the other simply for general oversight of farm animal welfare without legally mandated functions, the routing mechanism becomes very critical. The rule of thumb would be to err on the conservative side and send all "grey zone" proposals to the legally constituted IACUC. It should be obvious that for the smooth operation of a dual-committee approach, there must be good lines of communication between the two groups.

Just as there are good reasons for having only one review committee, there are valid reasons for forming a separate review committee for production agricultural situations. The following considerations support adding these duties to a totally separate farm animal committee.

1. **Utilizes Agricultural Expertise.** Most IACUC's have a limited agricultural representation, and members may be less familiar with recognized agricultural practices and standards. Having a separate agriculturally constituted committee can provide a wide range of expertise in evaluating programs and facilities and can provide firsthand knowledge about the various experiment station operations across the State.

**2. Reduces IACUC Workload.** Most IACUC's are heavily burdened already. Members have a sizable time commitment in reviewing protocols and facilities without additional responsibilities that are not federally mandated. Committee "burnout" is a real concern.

**3. Increases Flexibility.** Having a separate committee without governmental constraints gives the institution an opportunity to tailor the makeup and function of the committee to the institution's own unique needs. For example, an expedited review process for protocols involving noninvasive methods can be used extensively. In this situation, a review by one or two designated individuals may be sufficient and would reduce the overall burden on the committee. Reviews of facilities, programs, and formal reports to administrators could occur at less rigid intervals. Arrangements for the review of remote experiment stations could be tailor-made using ad-hoc members from the outlying areas. If the conventional IACUC were given the responsibility for these experiment station reviews, it would create severe logistical problems during semiannual review periods, particularly in large States such as Texas.

**4. Improves Agricultural Faculty Receptivity.** Having a separate committee for production agricultural animals would provide an opportunity to sensitize agricultural faculty members to the animal welfare issues without all of the mandated sanctions and potentially heavy-handed committee oversight which currently exists with IACUC's. Agricultural faculty are not accustomed to such intensive oversight and cannot be expected to welcome it with open arms. Trying to impose all of the IACUC-type requirements upon agricultural faculty in their teaching and research programs, without the backing of a Federal requirement, would be a thankless task indeed.

It is generally accepted that farm animal welfare should be an institutional concern. How that objective can best be achieved, however, is sure to stimulate active discussion. In the end, each institution must decide what is best for the local situation.

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***See also *Preparing the Farm and Farm Animals for Disasters* in the Disaster Planning section.***



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and accreditation programs targeted at ensuring proper animal care and use increasingly include agricultural animals. Also, public initiatives such as the Massachusetts ballot initiative to curtail animal agriculture and the Physicians Committee for Responsible Medicine's attempts to curtail the use of milk and meat in human diets were defeated by educating the general public. Various organizations have been developed to address animal care and use issues. The Animal Industry Foundation is a broad-based agricultural organization addressing animal rights issues. National biomedical organizations, the Foundation of Biomedical Research and the National Association for Biomedical Research, address education and governmental animal rights issues. State-level coalitions, such as those recently organized in Missouri, of agricultural organizations, academic research units, biomedical institutions, and agribusiness or consumer products companies offer great promise of educating others on animals rights and welfare issues. Animal scientists need to educate themselves on these issues, participate in their own institutional Animal Care and Use Committees, and help to educate the general public through organizations and programs at the local, state, and national level.

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AB- Animal science faculty teach, demonstrate, and ask students to perform procedures that are known to be painful. Potentially painful procedures include castration, branding, dehorning, ear notching, teeth clipping, beak trimming, comb and wattle removal, and tail docking. In each case, the degree of pain experienced by an animal is generally not known. Furthermore, the consequences of animals having to endure pain are also not fully understood. A survey was conducted of animal science faculty to identify current departmental policies and practices related to castration in beef and swine production classes.

Departments vary in what they require of students. Departments should set a policy to address 1) which (and how) potentially painful procedures are taught and 2) how the faculty deal with students who refuse to participate in putatively painful procedures. The institutional animal care and use committee should approve potentially painful teaching procedures after instructor and department have concluded that teaching such procedures is essential to a complete educational experience..

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## Useful World Wide Web Sites

### Farm Animal Council of Saskatchewan

<http://agri-infolink.com/facs/>

A comprehensive site that includes codes of practice for all farm animals.

### Livestock Conservation Institute

<http://www.lcionline.org/>



LCI serves as an umbrella organization with a diverse membership from virtually every segment of the food animal industry. LCI is a non-profit, consensus-building organization whose members influence the direction of research, product development and regulations related to food animal production.

**New Zealand Ministry of Agriculture and Fisheries**

<http://www.maf.govt.nz/MAFnet/issues/animal/codes.html>

Codes of recommendations and minimum standards for all farm animals and farm-reared deer.

**Pain**

<http://www.ahsc.arizona.edu/uac/iacuc/pain.shtml>

Species specific signs of pain in farm animals and other laboratory animals.

**Q Fever**

<http://www.ahsc.arizona.edu/uac/iacuc/special.shtml#qfever>

*Coxiella burnetii*, a rickettsial organism that is highly resistant to physical and chemical agents used in disinfection. It has been reported in most warm blooded animals including fowl. The most common source of infection in the United States is from sheep, although goats and cattle can carry the disease. This site is provided by the University of Arizona.

# **Wildlife and Field Research**





# Wildlife Research and the IACUC

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**[Editors note: USDA is in the process of revising the definition of field study. The final notice should be published sometime in Fall 1999.]**

The Institutional Animal Care and Use Committee (IACUC) is challenged with many duties under the Animal Welfare Act (AWA) and Public Health Service (PHS) Policy. Because of the diverse number of situations in which research animals may be used, regulatory agencies have appropriately shifted much responsibility for ensuring adequacy of animal care to IACUCs. The *Guide for the Care and Use of Laboratory Animals (Guide)* and the *Guide For the Care and Use of Agricultural Animals in Research and Teaching (Ag Guide)* provide both general guidelines and specific parameters for animal care and housing for traditional laboratory and farm animal species, respectively. Requirements for housing wildlife research animals (fish, birds, reptiles, amphibians, and wild mammals) and their use in research, however, are necessarily much less specific. The tens of thousands of species of fish, birds, amphibians, reptiles, and mammals makes specific guidelines regarding animal care difficult at best. Additionally, biological requirements for many species under study are not only unknown, but often are the subject of the study itself.

Each country, state, province, or local authority may have their own requirements which must be followed. The IACUC must apply the general principles contained in the AWA, the *Guide*, the *Ag Guide*, and the American Veterinary Medical Association (AVMA) Panel on Euthanasia to wildlife studies. The websites of the United States Departments of Agriculture Animal, Plant and Health Inspection Service (USDA-APHIS) and the Office for Protection from Research Risks (OPRR) contain a number of helpful policy interpretations and clarifications. Many professional societies and organizations have produced guidelines for the use of species with which they commonly deal. These are excellent supporting references for use by IACUCs to generate institution specific policies. Using these guidelines also leads to consistency in animal care across institutions, easing and improving investigator compliance as their institutional affiliation changes. Having clear, written policies and procedures reviewed by wildlife investigators and approved by the IACUC and the Institutional Official (IO), are essential in ensuring compliance by all individuals. Institutional policies should always be designed to obtain the desired outcome of both the PHS Policy and the Animal Welfare Act, i.e., humane care of all animals. Veterinarians and scientists trained with the species and procedures under review must always be involved in the development of IACUC policies.

Population dynamics, observational behavioral studies, disease pathogenesis and management, and effects of potentially negative environmental factors on wildlife populations are all common topics addressed in wildlife research at our institution. These all involve varying aspects of potential harm to animals being used in a research project. This article explores some of the challenges the attending veterinarian, the IACUC, and the investigator face when conducting wildlife research.



## When do I need to have IACUC review?

The most common question our IACUC receives from new investigators is what procedures require IACUC review? Several factors were considered when our IACUC developed our policy: the species and age of subject being used, the funding agency for the project, the affiliation of the individual with our institution, and the importance of animal care and use at our institution.

The point in development at which oviparous, ovoviviparous, and viviparous species become regulated animals had to be decided. The determination for viviparous was based on that of the AWA, at birth from the maternal animal. OPRR has ruled that birds become regulated animals once they have hatched from the egg. These concepts are easily transferred to ovoviviparous species, but less clear with many oviparous species. For fish, our IACUC has determined this same stage of development to be the "buttoned-up" stage, or when the embryo has fully absorbed the yolk sac and must forage on its own. Other IACUCs may choose an earlier point. As a result of our definition of when an animal becomes regulated, work with gametes and early embryos in fish is not regulated unless the animal is allowed to develop to or beyond the buttoned-up stage.

In enforcing the AWA, the APHIS requires IACUC review of *all projects which materially alter the behavior of animals under study*. The AWA only applies to warm-blooded vertebrate wildlife species. It considers simple, non-invasive capture and release procedures to not be covered under the AWA, and thus does not require IACUC review. Examples falling in this category might include taking measurements of various body parameters such as weight, length, blood sampling, and other general health indicators. Some forms of animal identification, such as tattoos, ear tags, and radio-collars, would also fall into this category. Any invasive procedures, such as surgical implantation of a transmitter, or housing animals for periods greater than 12 hours before being released require IACUC review, approval and oversight.

PHS Policy also requires IACUCs to follow AWA requirements. PHS Policy applies to all PHS conducted or supported activities involving live, vertebrate animals. In addition, the wording of an institution's Assurance may determine when IACUC review is required. Institutions must specify what projects conducted by their institution are to be covered by their Assurance. Because the University of Idaho has many production agriculture and wildlife research projects, our Assurance limits its coverage to PHS funded projects. However, if a non-PHS supported activity impacts on a PHS supported activity, then both projects must comply with the policy. According to a published interpretation of PHS Policy, "only when an institution can document that the animal care and use program funded by a non-PHS source is entirely separate and distinct, physically and programmatically, from PHS-supported activities will OPRR consider its exclusion from the Institutional Assurance."

It would be highly unlikely for a wildlife project conducted in the field to be funded by PHS. However, institutions may voluntarily require IACUC review for field projects to prevent the appearance of a double standard or that they are only performing IACUC review because it is legally required. To ensure appropriate care and use of all animals with which the University of Idaho is involved, our IACUC currently requires review and oversight of all projects involving University owned animals or performed by University personnel, regardless of who owns the animals, where they are housed, who funds the project, or whether they are reviewed by another IACUC. This is a common practice at academic institutions and is explained in our required introductory training sessions. This does require some additional paperwork for investigators and the IACUC, which understandably is not always appreciated.

Another factor investigators must consider is the journal(s) in which the investigator intends to publish his/her findings. Regulatory agencies and local IACUCs may not require protocol review, but more journals are requiring such review prior to accepting a manuscript for publication. A

written statement that such review has occurred has been common practice in biomedical research for several years, and has spread to many agricultural publications. This concept is also beginning to be recognized as an important process in wildlife publications. It is the investigator's responsibility to ensure that IACUC review and approval takes place when it is required by someone other than the IACUC, such as for publication.

### **Special Factors in the IACUC Review Process**

Many field studies reviewed by our IACUC are conducted in remote wilderness areas, either in the state, surrounding states, or at greatly distant sites. The committee relies on descriptions of the site by the investigator or knowledge of the study areas by committee members. Animal capture, handling, housing, surgical, and euthanasia procedures are evaluated in light of the location and local environmental conditions. The terrain, plant, and animal flora, day and night temperatures, predator/prey relationships, other species that may be inadvertently captured, and accessibility to the site are all considered. If significant variations from the AWA or PHS Policy are being sought, the investigator must justify the deviation. If the IACUC believes the request for deviation to be justified, a "variance" or "waiver" would be sought from the governing regulatory authorities prior to protocol approval by the IACUC. Planning ahead cannot be stressed enough when working with animal subjects that may only present sampling opportunities seasonally.

The committee will also evaluate potential hazards for the personnel working on the project including capture equipment used, handling of the species involved, prevention of zoonotic diseases, bite wounds, scratches, etc. When samples alone are provided to an investigator from another institution, the conditions of collection and care of the animals from which the samples originated are evaluated by the IACUC through a written description in the protocol.

Each protocol is evaluated on an individual basis weighing the relative benefits and risks involved. The same principles are applied to all vertebrate animals. We do not require protocol review for invertebrate species, but would apply the same considerations if an investigator were to request review of an invertebrate project. External funding agencies are relied upon for review based on scientific merit, but each project's goals are evaluated based on its relative merit to the species involved and society. This is especially important when dealing with endangered or threatened species, when potentially painful procedures are involved, and when the local ecosystem may be compromised.

### **Investigator Training**

All personnel must complete our IACUC training program for protocol approval to occur. Depending upon the procedures listed in a protocol, investigators and their staff may be required to complete additional training requirements. Written certification by qualified independent organizations, such as Safe Capture International, Inc. and qualified state or national wildlife veterinarians or other employees is accepted. When an independent certifier is not available, investigators must demonstrate competency to or be trained (such as surgical expertise) by the attending veterinarian or other qualified personnel for the procedures they wish to perform. This can often be done by performing/teaching the procedure on a related species in captivity.

Our occupational health program provides training on prevention of zoonotic diseases and immunization for tetanus. Those individuals working with wild carnivores may also receive rabies prophylaxis. All personnel who may come in contact with Hantavirus must complete Hantavirus prevention training including the use of a HEPA filtered respirator. When venomous animals are



being dealt with, investigators must keep on hand appropriate antitoxins. Protocols must be designed to limit the number of individuals exposed to potentially hazardous animals and materials. Investigators who have completed our IACUC training program are often delegated to provide training for non-affiliated field personnel that are working with animals on an approved project.

## **Capturing Wild Animals**

Almost all procedures conducted with wildlife require capture and use permits. IACUC approval is not granted until a copy of all required permits has been provided. The means of capture, the location in which captures are to be performed, the target species, the numbers of animals, the procedures which can be performed on the animals once captured, who can perform the capture and animal procedures, and the ultimate disposition of the animals as specified in various permits must be compatible with the information presented in animal care and use protocols.

The IACUC is staffed with one faculty member, and often two, with expertise in wildlife research and regulations. If there is any uncertainty regarding the need for permits, the IACUC will check with the Idaho Department of Fish & Game and the Idaho Division of Animal Industries. When animals or animal tissues are being imported, residents of the United States should consult with the United States Fish & Wildlife Service (USFWS), Department of the Interior (for Convention on International Trade in Endangered Species of Wild Fauna and Flora compliance issues), USDA-APHIS ( <http://www.aphis.usda.gov> ) (for potential animal pathogens), and the Center for Disease Control and Prevention ( <http://www.cdc.gov> ) (CDC, importation of primates and potential pathogens of human beings) for importation policies at the time of their study. The USFWS's web site ( <http://www.fws.gov/> ) contains a complete listing of state and federal wildlife handbooks.

## **Meeting Requirements for Housing and Inspection of Wildlife Animals**

Field projects may occur in remote wilderness areas, fish hatcheries, dams, privately owned facilities, or even facilities outside of the country. The AWA and PHS policy require all study areas and facilities used to hold AWA covered animals for longer than 12 hours to be inspected not less than every 6 months by the IACUC. As specified in the AWA, animal areas containing free living wild animals in their natural habitat need not be included in such inspection. By virtue of the PHS Policy definition of "animal facility," animals included under PHS regulations (but not the AWA) must be held for 24 hours or longer in study areas (satellite facilities) or be surgically manipulated in order for the site to require inspection. If an institution chooses to use less than 24 hours for all study areas, it should be reflected in their Assurance document.

It is often not practical or economically feasible to visit each of these remote sites. Since the University of Idaho has facilities throughout the state separated by 300-500 miles, we have added an ad hoc IACUC member who inspects facilities with the attending veterinarian at distant sites. Any committee member who wishes to participate in an inspection should not be prohibited. Waivers may be applied for with both PHS and USDA for special situations where site visits are impractical. IACUCs may also require a signed memorandum of understanding with the responsible authorities at associated facilities. Such agreements should not only address the care and use of animals, but the training required for animal care staff at these facilities, all budget items related to housing the animals and staffing the facility, and ownership of the animals for animal census reporting purposes and disposition of animals at the end of the project.

Wild caught animals may be brought into permanent facilities on occasion. The conditions for bringing the animals in are specified by the attending veterinarian for the facility. Serologic screening for diseases of concern may be required. Factors considered include the current disease status of animals in the facility, the type of housing available in the facility (filtered exhaust air, isolation cages, barriers, etc.), the disease status of the animals entering the facility, the biological requirements of and temperament of the animals to be brought into the facility, and qualifications of animal care staff at the facility. Investigators, facility managers, and veterinarians must be creative in developing environments which meet the biological needs of the animal and regulations. With some species, deviations from regulations may be required to meet the biological needs of the animals. Waivers from USDA and/or the NIH, Office for Protection from Research Risks should be sought prior to protocol approval.

Unless an animal is an endangered or threatened species, its return to the wild is usually discouraged to protect the existing population from diseases acquired unknowingly in captivity. The disposition of animals is normally specified in capture permits, which have ultimate control.

### **Refinement of Protocols**

Because of the cost and difficulty in acquiring wild animals, investigators always try to obtain as much information from one animal as possible. A museum of dead animals and animal parts is maintained with representative samples of species being used in research. Museum specimens are for use in undergraduate and graduate courses, public education programs, and possibly in future research projects. These specimens are often animals euthanized or killed during another project, rather than just for use in the museum. Samples may also be taken and used for karyotyping in other population studies.

Identification and capture techniques must always be the least invasive possible. Requested animal identification methods are evaluated using the same criteria as the investigator most likely used when designing the protocol. Does the individual animal need to be identified, or just as a member of a group? How long does the identification need to remain in place? Will animals be released after identification and identified from a distance, or is recapturing necessary? How aggressive is the species of animal(s) being dealt with? What is the likelihood and necessity of being able to recapture the same animal? How painful is the method of identification? These are all concerns IACUC members consider and weigh against the benefits of the research. Tattoos, hair clipping, radio-collars, ear tags, and other non-invasive methods would be preferred over surgical methods such as toe clipping. The same criteria for surgical procedures used in biomedical research would be applied to wildlife situations. Unless scientifically justified in the protocol, the procedure would need to be performed aseptically and under anesthesia with post-operative analgesics administered.

Live trapping, such as mist nets and Sherman traps, is preferred. The frequency and difficulty of checking live traps, when traps are set and closed, protection from adverse environmental conditions and predators, and provisions for food and water for infrequently checked traps are all considered. Snap traps and other lethal traps may be approved when indicated. The investigator would need to justify the use of lethal traps through the scientific design of the protocol or the elimination of potential health risks to the investigator. This would include health risks associated with removing animals from traps and the euthanasia process. Protocols should also include provisions for dealing with accidental/incidental injuries to animals in traps.



The euthanasia method used must be in compliance with the AVMA Panel on Euthanasia, unless justification is provided in the protocol and approved by the IACUC. Volatile gases in closed containers are preferred in habitats where plague, Hantavirus, or other parasite or aerosol transmitted diseases are likely. Cervical dislocation without anesthesia must be justified in the protocol. Gun shot of an appropriate size for the species and by qualified personnel is accepted when other alternatives are logistically prohibitive. An example would be the capture and euthanasia of large ungulates, such as deer and elk, that will be euthanized as part of a project in very remote locations and steep terrain.

## Summary

IACUCs are faced with difficult challenges in striking a balance between animal well-being and scientific discovery with regards to wildlife research. The unique environments in which wildlife are found, their biological characteristics, the safety of personnel, and appropriate regulations must all be considered when performing and monitoring wildlife research. A joint effort of cooperation and discovery is essential between investigators, IACUCs, and regulatory agencies to overcome these challenges.

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# Safe, effective, and humane techniques for euthanizing wildlife in the field

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Resource managers across the national park system are occasionally faced with the need to destroy wildlife species for a number of reasons, such as protection of endangered species, protection of the public health, and population control of species.

When choosing euthanasia techniques as part of a resource management program, managers must select techniques that are humane for the species being euthanized, safe for personnel carrying out the procedure, not dangerous to park visitors or nontarget species, and appropriate for the location and feasible within personnel and budgetary constraints.

In selecting a euthanasia technique, the manager must first consider that the technique is efficient and humane for the target species (American Society of Mammalogists 1987). The universally accepted standards for these criteria are found in the 1993 Report of the American Veterinary Medicine Association (AVMA) Panel on Euthanasia (American Veterinary Medical Association 1993). These techniques fall into three general categories: injection (barbiturates), carbon dioxide, and gunshot. Whichever of these techniques the manager selects must be species-specific and correctly performed by trained personnel to be safe and effective.

Euthanasia by the injection of barbiturates (e.g., sodium pentobarbital) is perhaps the most humane euthanasia technique, and it is suitable for most species, safe for personnel performing the procedure, and moderate in cost (Fakkema 1994; Grier and Clovin 1990; American Humane Association 1988). Barbiturates are one of the cheaper euthanasia agents. However, as a controlled substance, the use of barbiturates requires a permit from the Drug Enforcement Administration, secure storage, and veterinarian supervision. The animal must be restrained during administration (e.g., squeeze cage) and personnel performing the procedure must be skilled. Dosages must be correct for the species and the animal's weight. A park's maintenance staff may construct squeeze cages of their own design or by using designs found in the literature. If a veterinarian is not on staff, one may be available from a nearby humane society or a local vet may be willing to consult as a nonpaid volunteer.

Another effective, humane, safe, and inexpensive euthanizing technique is carbon dioxide (Erickson 1994). This technique works well for most animals; however, some species and neonates may have some increased tolerance to carbon dioxide. Because carbon dioxide is heavier than air, care must be taken to completely fill the chamber before exposing the animal to the gas. This is of special concern with tall or climbing animals. Carbon dioxide is low cost. Supplies include a carbon dioxide canister, carbon dioxide, appropriate plumbing, and a chamber that can be constructed by park personnel. The main disadvantage of this technique is that it may not be suitable for remote or inaccessible locations due to difficulties transporting heavy carbon dioxide canisters.

If done properly by trained personnel, gunshot may be used as a humane form of euthanasia. For each species, the shot must be fired at a specific site on the animal to assure rapid death.



(Australian Veterinary Association 1987; Longair et al. 1991). One danger of this technique is that a bullet may ricochet off the substrate or cage and injure the shooter or others. The shooter must also have adequate eye and hand protection due to the possible danger from blood-borne pathogens. Additionally, there may be legal reasons why a manager may not want to use firearms in a park.

Managers wishing to learn more about specific euthanasia techniques are encouraged to consult the resources cited in this article or attend a euthanasia seminar sponsored by an organization such as the American Humane Association. For a summary of humane euthanasia techniques see table 1.

Table 1--Humane euthanasia techniques\*

Method	Advantages & Disadvantages	Cost
<b>Injection</b> Barbiturates	Most preferred method of euthanasia Suitable for most species. Safe for personnel performing procedure. Requires DEA permit, secure storage, and veterinary supervision. Requires squeeze cage, which may be easily constructed by park personnel.	Moderate
Carbon Dioxide CO <sub>2</sub>	Works well for most species. Some species and neonates may exhibit increased tolerance to CO <sub>2</sub> . Special care must be taken with tall or climbing animals to completely fill the chamber before exposing the animal. CO <sub>2</sub> chamber may be easily constructed by park personnel. Safe for personnel performing the procedure. May not be suitable for remote locations due to weight of CO <sub>2</sub> canisters.	Low
Gunshot	Firearm must be of appropriate caliber and impact for species and must be delivered to specific site on animal. Requires skilled marksman. Possible danger to shooter from ricochet. Possible legal constraints in some parks.	Moderate
*All methods can be humane and safe if administered by properly trained personnel		

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## Useful World Wide Web Sites

**American Society of Mammalogists, Animal Care and Use Committee**

[http://asm.wku.edu/committees/animal\\_care\\_and\\_use/ancarecomm.html](http://asm.wku.edu/committees/animal_care_and_use/ancarecomm.html)

The sustaining goals of the Animal Care and Use Committee are to serve as a liaison to society members on matters concerning the care and use of wild mammals, to assist in the interpretation of

new or revised governmental regulations, and to provide government and non-government agencies with reasoned, professional advice on matters of animal care and use of wild mammals.

**Arizona State University, Handling Hantavirus**

[http://researchnet.asu.edu/animal\\_care/hantavirus.html](http://researchnet.asu.edu/animal_care/hantavirus.html)

Guidelines for wildlife researchers.

**New South Wales Agriculture, Animal welfare guidelines**

<http://www.agric.nsw.gov.au/Aw/Guideline/>

This site is provided by the government of New South Wales, Australia. Topics include: draft guidelines for the use of pitfall traps; guidelines for animal care and ethics committees (ACECs) supervising research on captive wildlife; guidelines for collection of voucher specimens; guidelines for opportunistic research on free living wildlife; individuals and institutions engaged in collaborative research.

**University of Florida, Animal Care and Use**

<http://nersp.nerdc.ufl.edu/~iacuc/wildlife.htm>

This site provides access to rules and regulations that govern wildlife research at the University of Florida.



# Statistics and Animal Numbers







# Reducing Animal Numbers: Sequential Sampling

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How much is it worth to be able to cut the number of animals needed in an experiment in half? Is it worth you reading on?

One way of reducing the number of animals needed in an experiment is to use more sophisticated statistics, not a more difficult method, in fact less difficult once you know how. I'll describe a technique enabling you to shave the number of animals used by about 30-40 percent or more and to do your statistical analyses faster and easier.

"What is the cost of all this generosity?" I hear you ask. To have all these advantages you must have some estimate of three things: your control/baseline mean, control/baseline variance, and the effect size. You will most likely have all of these already, but you will need to use them in a slightly different way than you have in the past.

## Intuition

There are three ways to decide on the number of subjects to use in an experiment, and I will describe them in descending order of their efficiency (and their ethical nature). The first is to use one's intuition, an estimate, an educated guess if you wish. It is well known by now that these subjective estimates of the number of subjects needed are usually overestimates.

Try a test on yourself to see if you have been or would be incorrect in your estimates of the numbers of subjects needed: Most people are aware that the intelligence quotient (IQ) is devised so that it has a mean of 100 and a standard deviation of 15. That means that if you take a random sample of people, the mean of their IQs will be close to 100. To give some feeling for the IQ, the mean of students at university is higher, about 120; genius is 130. Having a standard deviation of 15 means that 68 percent of people fall within 15 points of the mean plus or minus; in other words 68 percent of people have an IQ of between 85 and 115. Ninety five per cent of people have an IQ that falls within two standard deviations (30 points) of the mean. That is one of the valuable characteristics of the standard deviation, having 95 percent of the sample within two standard deviations of the mean.

With that in mind, if I said I had found something that would raise someone's IQ 30 points (or 20 points, or even 10 points), how many subjects do you feel you would have to test in order to come to a statistical decision at the 0.05 level for each of these three problems? To make it more realistic, a drug company has offered to pay you a lot of money for this substance that you claim will raise IQ, but you will have to pay them a lot before they start. Therefore you don't want to say it increases IQ if it doesn't as that will cost you a lot, nor say it doesn't if it does as you will miss out on a lot of money. Let's say the substance also causes side effects. So, you don't want to overestimate the number of subjects needed to be sure of detecting a difference, or underestimate to be cautious. If you have underestimated, you might miss something important. If you have overestimated, you might be exposing some of your subjects to unnecessary suffering. How many subjects do you think

you would have to give the drug to see if the substance works? Give your estimate: (a) for an increase of 10 points = \_\_\_\_, (b) for an increase of 20 points = \_\_\_\_, (c) for an increase of 30 points = \_\_\_\_.

The true values are given in the last line of this paragraph. I predict you will have overestimated especially in the condition when the effect was the most extreme, the 30-IQ-point condition. The answer for 10 points is 20 subjects, for 20 IQ points is 5, and 30 IQ points needs only two subjects to detect the difference.

When most of us are planning an experiment, there is more involved than just guessing. Normally, we decide on the number of subjects based on (a) how many subjects there are available, (b) the cost to us, or to them, of the test procedure, (c) and finally that feeling about how many we will need to make the sort of decision that we hope to make. If there are few subjects available, testing is costly or distressing to subjects, or we feel the effect we want to show is a big one, then we use fewer subjects. If there are lots of potential subjects, testing is quick or perhaps even beneficial to the subjects, or the effect that we are trying to detect is a tiny one, we select more subjects.

A common question that is posed by students or experimentally-naïve colleagues is, "How many subjects do I need?" The answer still most commonly given is, "As many as I can afford to test."

## Power Analysis

The second way to decide on the number of subjects needed is to do a power analysis. This technique is more efficient when compared with the estimate described above in that fewer subjects are required in order to arrive at a decision with the same degree of certainty. I did a power analysis to arrive at the figures used to answer the three questions above, those about how many subjects would be needed to see if the compound raised IQ.

A few of the existing statistical packages will compute the number of subjects needed with varying degrees of ease. Here, I have used STATISTICA by StatSoft (5) and I found it easy to use. Power analysis is hidden away in the Process Analysis section of STATISTICA. You may find it of interest to know that power analysis (and sequential sampling, described below) is commonly used by "quality control engineers...to determine how many items from a batch to inspect in order to ensure that the items in that batch are of acceptable quality." (5, p. 3,571).

To use the technique, you need to know three things: First, you need to know the comparison mean, the mean of the control group. In our example above the mean was an IQ of 100, but it could be the average number dying under some treatment, the percentage normally infected, the amount of pain under some procedure, the average frequency or duration of aggression without the recommended intervention, etc.

Second, you need some measure of variability, generally the standard deviation. We used the value of 15 in our IQ example as it is widely known. If you have a mean for your comparison condition, you will usually already have a measure of variability.

Your third requirement is an estimate of effect size. We are not ordinarily asked for an estimate of effect size, but we often have one in mind. To use the IQ example again, if our substance only increased IQ by one point, and even if the effect were statistically significant, we would say that the substance was not valuable, that the effect size was so small as to be uninteresting, that no one would buy it. We know that an extremely small effect size is worthless.

There are a number of things that can help in determining effect size. The most common is other research. I carry out research in the area of environmental enrichment, formerly with monkeys and more recently with farm animals (1). One difficulty in that area is deciding on an appropriate effect size, and I know of no research where anyone has reported estimating effect size.

Change is easy; improvement is easy too. Almost anything you do to a monkey alone in a zoo enclosure, to a rat living in a bare laboratory cage, or to a pig farmed in a small crate will produce a change in their behavior. But is that change large enough to be important, large enough to be worth the expense to make that change? Is the improvement to the welfare/behavior of chickens large enough to warrant the cost of increasing the cage size?

Other help in determining whether an effect size is sufficiently large to be important is *percent of variance accounted for*. This is measured by  $r^2$  in correlation and by omega-squared ( $\Omega^2$ ) in analysis of variance.

Recently, I have been assessing the effects of visual shelter on levels of stress and aggression in farm animals. Now, if planting a row of trees will reduce aggression in deer, as it will (8), will you the farmer plant the trees? Before speculating on an answer, you might be excused for asking (a) the cost of the trees and (b) the degree to which the aggression will be reduced--that is, the cost/benefit analysis. The benefit question is the same question the researcher must ask him/herself to get an estimate of effect size. How big a reduction in aggression must I find before I conclude there are benefits in providing visual shelter?

The literature suggests that in monkeys, in bulls, and in rats, providing a visual barrier behind which some of the animals can hide will reduce aggression by about 50 percent. We might set our effect size near that value. Using that value, we can then calculate the number of subjects we need to test to see if visual shelter reduces aggression by at least half in deer. (In case you're interested, it does.)

The program STATISTICA asks for the mean under the null hypothesis (IQ=100), the standard deviation (IQ=15), the effect size (IQ=130 in our example above). It also asks for the alpha level (conventionally  $p=0.05$ ), the beta level (conventionally=0.1), and whether the predictions are one- or two-tailed. After you enter these numbers, STATISTICA presents you with the number of subjects you will need to test--sounds easy.

Then you carry out your experiment, do your test for statistical significance (for example, t-test or ANOVA), and draw your conclusions. But there is an even easier method and one that is even more powerful.

## Sequential Sampling

The third and best way to decide on the number of subjects that you will use in an experiment is called sequential sampling or the sequential experiment. While in the above examples the subject size was either estimated or calculated and then fixed before the experiment was carried out, *in the sequential experiment the number of subjects to be used is undecided and is determined only by the sample observations as they are completed*. That is the only difference between sequential sampling and the power analysis described above. You test one subject, look at his data, decide, test another subject, look at her data, decide, and so on.

In the fixed sampling experiments we all are familiar with, there are two possible decisions we can make: Either reject the null hypothesis and then conclude the groups are different, or fail to reject the null hypothesis and by default accept an alternative hypothesis, usually concluding the groups are not different. In the sequential experiment there are three possible decisions. The first



two are the same as above, but the third is a different one: Either keep sampling, or stop sampling and conclude that a decision about the null and alternative hypotheses cannot be made. In other words, more samples are needed before a decision can be made as to whether the two groups differ or not.

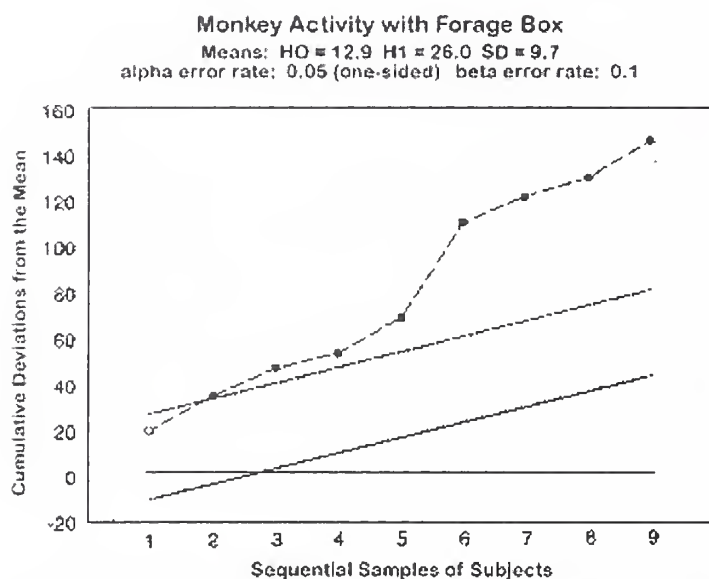


Figure 1. Cumulative deviations from the control mean in activity by nine individually housed Cotton-top tamarins.

This third alternative, let's call it the devil's alternative, is likely only when the variability is large and the difference between the means is very small. This condition is the only penalty of using sequential sampling, other than having to have an estimate of effect size.

To actually employ sequential sampling, you need only have the same equipment as for the power analysis--mean, variability, and effect size. You can enter these values into STATISTICA and, instead of pressing the *fixed sample* button, you press the *sequential sampling* button. The graph in figure 1 is produced.

To illustrate, we will use some real data and superimpose that data on the graph, just as one would do in reality. The only difference is that I have already tested all the subjects, whereas in a sequential sampling experiment, one would only test one or two subjects at a time. We will return to a monkey enrichment experiment I did, illustrated in a widely displayed video (6). To test to see if a small forage box would improve conditions for individually-housed marmoset monkeys, I decided that the monkeys would have to be more active, in fact at least double the levels of activity when monkeys live in a bare cage without the ability to forage. The control or baseline levels for a group of monkeys living singly in bare cages was 12.9 percent of the day spent active (with a standard deviation of 9.7). Our effect size of doubling means that with the forage box, they must spend at least 26 percent of the day active for us to conclude that the effect of the forage box is important.

To restate the techniques that I could have used to decide how many subjects to use: I could just guess how many to use. How many monkeys would you say I would need to use in order to see if the forage box increases total daily activity? Answers please, now \_\_\_\_\_. I would have estimated a minimum of 15 but only 13 were available to test at baseline; this further decreased to 9 by the time of the retest. I could have done a power analysis, so I have done one now. In the power analysis, STATISTICA helps us calculate that we would need nine monkeys. Or I could have used sequential sampling, and I have done this in detail below.

The following is the procedure for sequential sampling. To see if the manipulation is significant at the prescribed effect size, you simply graph your data. To do this you give STATISTICA the information we have already ascertained, namely mean, standard deviation, and effect size, and it will produce the figure reproduced here (fig. 1). Superimposed on the graph is the data I actually obtained. STATISTICA will plot that data too if you have it. The sequential sampling plan produces a graph on which there is one parallel corridor (a two-tailed test has two corridors) leading gradually away from the baseline of "no difference." You plot the mean obtained from each subject in turn, actually the deviation score for that subject from baseline. If that plot

remains within the corridor, it means that you can neither conclude that your forage box is effective nor that it is useless, that is, you should keep sampling. If the plot drops below the corridor you can conclude that behavior with the forage box is no different from the control condition; if the plot goes above the corridor, you conclude the forage box is effective in improving behavior, that is reject the null hypothesis.

In the example we have used, I could have tested just one subject and plotted her data on the graph. You can see if that subject's improvement score had been over 30, that is if the subject had increased her score from the baseline mean of 13 to at least 43, her score would have fallen above and outside the corridor and I would have been able to stop testing and then conclude that the forage box had at least doubled activity and the effect was significant at  $p=0.05$ . In fact her score was only 33, having improved 20 points above baseline, and that score of 20 is plotted on the graph. The second monkey had a score of 28, 15 above baseline, and so 15 is plotted. The cumulative scores of the two monkeys now extends above the corridor, just above the corridor, and testing can be stopped.

To arrive at a decision with the same degree of certainty as I did with just 2 subjects using sequential sampling, I would need to have tested 9 subjects had I done a power analysis, and I would have used 15 had I gone by my own intuition based on over 30 years of research with monkeys. You can see that a power analysis will reduce the number of subjects used by almost half, but the sequential sampling technique reduces the number needed even further. In this example, sequential sampling reduced the number of subjects by 70 percent from the power analysis and even more from my educated guess.

Why such a huge reduction? If the forage box had improved behavior only by the bare minimum allowed, 13, it still would have taken only 4 subjects before going outside the corridor. But because the box was so effective, almost trebling the amount of activity, the scores rapidly exceeded that corridor of "no significant difference." That is one of the unexpected benefits of sequential sampling not found in any form of fixed sampling. In the case that the effect size is even greater than postulated, even fewer subjects are needed.

Imagine that in the study described above, the experimental manipulation was a painful one. We would want to know if it worked but would also wish to keep the subjects used to a minimum in case it was not effective. Or we might want to minimize subject use because we wanted to know if the compound was toxic. In this example, I should use only two subjects and could if I use sequential sampling. To reiterate, in almost all cases, sequential sampling procedures are preferable to fixed sampling procedures because sequential sampling is more powerful in that fewer subjects are required in order to arrive at a decision with the same degree of certainty.

## **Ethical Considerations**

Is it unethical not to use sequential sampling if it is appropriate to use it? I would argue that it is unethical. If you are carrying out a procedure in which you wish to use the fewest animals possible to come to a conclusion with a desired level of confidence, you should use sequential sampling unless there are good reasons not to do so. To paraphrase, this is a technique to reduce to an absolute minimum the amount of distress imposed on animals.

Why don't ethics committees insist on it? Probably because they have never heard of it. Until recently, the computations to calculate power and sequential sampling have been tedious, and the technique has not been described in textbooks. STATISTICA has changed all that.

Do you want to read more about sequential sampling? The math-phobic can read about these techniques in a chapter by Edwards (2), the behavioral scientist in a friendly text by Leavitt (3), the stats-sophisticate can consult Pyzdek (4) or go back to the man himself, to Wald (7), and finally

the statistics package STATISTICA (5) will take the practitioner quickly and painlessly through the mechanics of actually computing the numbers. I was unable to find procedures for sequential sampling in other commonly-used statistical packages.

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# Statistics and Animal Numbers Bibliography

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AB-Laboratory mice, rats, and rabbits may harbor a variety of viral, bacterial, parasitic, and fungal agents. Frequently, these organisms cause no overt signs of disease. However, many of the natural pathogens of these laboratory animals may alter host physiology, rendering the host unsuitable for many experimental uses. While the number and prevalence of these pathogens have declined considerably, many still turn up in laboratory animals and represent unwanted variables in research. Investigators using mice, rats, and rabbits in biomedical experimentation should be aware of the profound effects that many of these agents can have on research.

Descriptors: bacterial infections, parasitic diseases, rodent diseases, virus diseases, microbiology, mice, rabbits, rats, reproducibility of results, epidemiology, immunology, parasitology, virology.

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AB- One hundred and thirty-three papers (80 Original Articles and 53 Short Contributions) of 279 papers in 23 consecutive issues of the Australian Veterinary Journal were examined for their statistical content. Only 38 (29%) would have been acceptable to a statistical referee without revision, revision would have been indicated in 88 (66%), and the remaining 7 (5%) had major flaws. Weaknesses in design were found in 40 (30%), chiefly in respect to randomisation and to the size of the experiment. Deficiencies in analysis in 60 (45%) were in methods, application and calculation, and in the failure to use appropriate methods for multiple comparisons and repeated measures. Problems were detected in presentation in 44 (33%) of papers, with insufficient information about the data or its statistical analysis and presentation of statistics (appropriate missing or inappropriate shown) the main problems. Conclusions were considered to be inconsistent with the analysis in 35 (26%) of papers, due mainly to their interpretation of the results of significance testing. It is suggested that statistical refereeing, the publication of statistical guidelines for authors and statistical advice to Animal Experimentation Ethics Committees could all play a part in achieving improvement.  
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NAL call number: QL55.A1L3  
AB- The purpose of this study was to determine if the subcutaneous chamber technique would reduce the number of rabbits required for antisera production by enabling serial use of individual animals for multiple antigens. Rabbits were assigned to immunization protocols against two antigens in series that involved combinations of chamber implantation, Freund's adjuvant and injection of antigen either by the subcutaneous route or by direct inoculation into the chamber. Results indicate the systemic immune response to both antigens achieved similar magnitude and duration by use of either Freund's adjuvant or direct inoculation of antigen into the chamber, suggesting that chamber use may be able to replace use of Complete Freund's adjuvant for many antigens. Rabbits re-used for a second antigen were equally successful in production of significant titres in both serum and chamber fluid without evidence of either a significant inflammatory response due to the chronic presence of the implant or a decrease in the yield of antisera harvested from the chamber. These results support the advantages of chamber use as reported by others and demonstrate that the chamber technique can significantly extend the productive life of an individual animal that would otherwise be euthanized following a single use in antisera production.  
Descriptors: rabbits, immune serum, biological production, antigens, antibody formation, yields, hemocyanins, adjuvants, cholera, bacterial toxins, containers, implantation, animal welfare, alternatives.

## Useful World Wide Web Sites

### Guidelines for Determination and Justification of Animal Numbers

<http://www.rgs.uci.edu/rig/asnumber.htm>

Topics included in this site provided by the University of California at Irvine are: overview, basis, study design, pilot studies, inclusiveness, alternative methods, inbred animals, repetition of experiments, modification of approved animal number, and references.

### **Statistics Justification**

<http://nersp.nerdc.ufl.edu/~iacuc/statistics.html>

This site is provided by Animal Care & Use at the University of Florida.

# Disaster Planning







# Disaster Planning For Animal Facilities

The U.S. Department of Agriculture gratefully acknowledges the Florida Animal Disaster Planning Advisory Committee (ADPAC) for permission to use the following article and checklist. Their web site is at <http://www.fl-adpac.org/>

*ADPAC is an ad hoc group of organizations and individuals interested in promoting the effective development and implementation of disaster plans to protect animals. The group was organized after Hurricane Andrew killed, injured, and displaced tens of thousands of dogs, cats, horses, cattle, birds, exotic pets, and other animals.*

*ADPAC is not a formal legal entity. Its members seek to open lines of communication among the various animal groups in the state, and with governmental entities that develop and implement disaster plans with the goal of protecting human lives and property. It is the belief of ADPAC that the plans for humans and animals must be intertwined if either are to be effective.*

*If you would like information on ADPAC, contact Laura Bevan, Southeast Regional Office Director, The Humane Society of the United States, 1624 Metropolitan Circle, Suite B, Tallahassee, FL 32308, call (850) 386-3435, or e-mail [lbevan@unr.net](mailto:lbevan@unr.net) for more information.*

## Introduction:

It is vital that animal facilities prepare for disasters, not only for the animals housed inside, but so that the facility will be viable in the aftermath. These facilities will include animal shelters, kennels, veterinary clinics and hospitals, pet shops, horse stables and other facilities where animals are routinely housed. The following guidelines are appropriate for all and will help determine which disasters and dangers a facility may be vulnerable to, and what plans they can make now to mitigate damage and downtime.

## Evaluate your Animal Facility

A. Know the dangers of the facility's location. Are you:

- ▶ in a storm surge area for hurricanes of any category?
- ▶ in a flood plain for nearby lakes, creeks or rivers?
- ▶ located near any hazardous waste plants or disposal sites?
- ▶ near any railroad tracks with trains carrying hazardous wastes?
- ▶ near any interstates that have trucks carrying hazardous wastes?
- ▶ near any fuel depots?
- ▶ in an area prone to wildfire?
- ▶ near any area with earthquake faults?
- ▶ in an area that a power outage could create a heat or cold emergency?
- ▶ Fire: we all run the risk - our most common and deadliest single disaster. Check with your local emergency management department or fire department for assistance in assessing the potential disasters in your area.

B. Know the dangers of the actual structure:

- ▶ What is the building made of (wood, concrete, brick, etc.). Is it solid enough to withstand hurricane force winds?

- ▶ Does it have sliding glass doors, large windows or a large number of windows? Do these have hurricane shutters or appropriate coverings for heat or cold emergencies?
- ▶ If the facility has kennels, are they indoor/outdoor runs or all indoor?
- ▶ What areas of the facility would be safe in a hurricane or tornado? Are there interior areas that would be protected?
- ▶ Is the roof secure? Is it hurricane clipped or strapped? Is it capable of water loading from heavy rains, snow or ice?
- ▶ Do you have exposed, overloaded, or old electrical wiring that could start a fire?
- ▶ Does the facility have a number of fire extinguishers, and are they in convenient and easy to locate?
- ▶ Do you have smoke detectors throughout the facility, and are the batteries checked at least twice a year? (An alert system and sprinklers are preferred.)
- ▶ Do you allow smoking in or around the building? If so, is a proper smoking policy in effect?
- ▶ Is the area around the facility cleared of underbrush and trees to prevent wildfire from spreading to the building?

It would be advisable to have the building properly evaluated by an engineer or another professional experienced with the requirements necessary for a facility to withstand a major disaster. Check with your emergency management department to see if this is a service it provides or if it can recommend a professional.

## **Insurance**

Is your insurance adequate to cover all losses? You need to properly evaluate your coverage at least once a year.

- A. Identify your facility on the flood plain and or storm surge map located at your local Emergency Management Department.
- B. Make a complete inventory of the property, including photographs of each room. Store this written or videotaped inventory with insurance papers in a safe place, keeping a duplicate inventory file off-premises.

## **Set Priorities**

- A. Identify the most expensive or irreplaceable items (the animals in the facility will be your top priority) and create plans to preserve and protect them.
- B. Identify what items are most necessary to get the facility operating again. (i.e. records, equipment, etc.)
- C. Movable Inventory (i.e. animal control trucks, cars, etc.) - make arrangements now for a safe location where these items can be moved well in advance of the storm. Make sure your vehicles are not moved to a location where they can be immobilized, such as by falling trees, flying debris, or flood waters. Tie them down if appropriate.

D. Move important inside equipment to the center of the room as high as possible (upstairs if available) and wrap it with waterproof tarps or plastic. Secure with a rope or tape. Anchor downstairs furniture.

E. If you are in a floodplain, make arrangements to move as much as possible from this location well in advance.

F. Glass - Shutter or board all glass to prevent it from flying around doing additional damage or injury. Whenever possible, large windows or sliding glass doors should be covered with commercial hurricane shutters, since it is difficult for them to be properly boarded. In case of wildfire, remove drapes when one threatens to prevent them from catching fire as the glass becomes heated.

G. Contact your local fire service and ask them to do a fire drill at your facility so they are familiar with where the animals are housed. Also ask them to do a walk through to point out situations which might be fire or chemical hazardous.

H. Install a fire alarm system, if you do not already have one. Have it connected directly into the fire department. By the time an internal alarm is heard, it could be too late.

I. Have fire extinguishers readily available throughout the facility and make sure all employees know how to operate one.

J. Install a lightning suppression system.

K. If in a wildfire prone area, keep hoses attached on all sides of the building with lawn sprinklers for wetting down roofs.

## **Create a Pyramid of Employee Release**

A. Release all non-essential personnel as soon as possible so they can assist their families in making preparations. See that all employees have written personal disaster plans covering their home, family and pets - if they are prepared, they are better able to concentrate on assisting in getting the facility prepared effectively.

B. Release second level of employees as soon as they have completed their assigned disaster preparation duties.

C. Remaining employees leave as soon as premises are prepared and secured. Always start well in advance - the key to minimize damage and injury is evacuate as quickly as possible. All employees should be released in time for them to reach safe shelter. In the case of hurricanes, this should be before sustained winds reach 45 mph.

D. Explain:

- ▶ Watch: generally issued 72 hours prior to an expected event - preparations should begin at that time. The radio should be monitored constantly.



- ▶ Warning: generally issued when the expected event is imminent within the next 24 hours or sooner. Depending on when the Warning is issued (day, night, weekend) your plan may change dramatically. Depending on your operating hours you may have to plan to call in key employees to prepare the facility. Home phone numbers should be kept with the manager or director at all times. Also call non-essential employees and tell them not to report to work until further notice. Have a plan to recontact employees if telephone lines are inoperable.

E. It is not recommended that you demand participation of employees in responding to the aftermath of a disaster. Your disaster plan could fall apart if you depend on certain people who are not available because of family concerns.

F. Recognize in developing the personnel section of your disaster plan that even those employees who make a commitment to assist before or after a disaster may not be able, for reasons beyond their control. Cross train employees in disaster duties.

## **Specific Preparations**

### **A. Hazardous Materials**

- ▶ Make sure all hazardous materials are labeled - if they do get washed away or strewn about your local clean-up crews will know what they are dealing with.
- ▶ Attach all outside storage cylinders to the building (attach at top and bottom); if attached at only one place, cylinders can be battered against the building and possibly break valves. Remember, nothing is too heavy to worry about!
- ▶ If small quantities of hazardous materials are stored on open shelves, make sure the shelves have adequate lips to keep materials on the shelves. Make sure cupboards are fitted with positive latches.
- ▶ Separate all incompatible chemicals!
- ▶ Keep up-dated inventories of all hazardous materials - store this in a safe place off premises or take it with you upon evacuation.
- ▶ Shut down the valves on all tanks before leaving.

### **B. Records**

- ▶ If possible, put vital records on hard disk to be taken along when leaving, or electronically transfer all important records to a location outside the expected disaster area.
- ▶ If records are not computer compatible, place them inside plastic bags and then pack in boxes.

- ▶ Seal the boxes with tape.
- ▶ Mark the outside of the box with pertinent information, such as department name and/or name of supervisor responsible for records.
- ▶ If records are confidential, indicate this on the outside of the box.
- ▶ Take boxes to a central location to receive an assigned number and to be inventoried.
- ▶ Remove boxes to a safer location outside of the disaster area - this location should be pre-determined.

C. Assign employees to clear outside area of all loose objects. Remove flags from poles as this substantially increases the ability of the flagpole to withstand wind.

D. If the shelter has any refrigerated inventory (drugs, medicines, etc.) immediately set all refrigerators to the lowest setting. However be aware that once the power is off refrigerated items generally will stay cold for approximately 48 hours. If the power outage is expected to be longer than this, or if the items will otherwise be lost, relocate them or donate them to relief efforts.

E. Drive any motor vehicles to a safe location, if there is none at the facility. Make sure the vehicles are fully fueled, since gas stations will be unable to operate due to lack of power.

F. Empty freezer of any dead carcasses and dispose of properly. Turn freezer on as cold as possible for holding of dead animal bodies immediately after the disaster.

## **Final Securing of Premises**

A. Contact your alarm system company and local officials advising that you are shutting down operation of the facility.

B. Provide employees' with appropriate identification showing employment or relationship to the animal facility so that they will be able to return after the storm.

C. Unplug all equipment and turn off electricity at breakers before leaving - including air conditioning, water heaters, gas and water (this helps prevent contamination).

D. Recheck valves on hazardous materials tanks to make sure they are fully closed.

## **Returning after the Disaster**

A. Avoid all metal as it may be energized. Wear rubber boots and rubber gloves.

B. Enter with extreme caution; check structural integrity. Always use a buddy system when entering the structure.

- C. Don't strike matches, as gas leaks or leaks of other hazardous materials are common. Use flashlights only.
- D. Make a written assessment of the building and its contents. Photograph as similarly to the original inventory photographs as possible, to expedite insurance processing.
- E. Make any safety repairs immediately that are necessary to protect employees and minimize further damage.
- F. If there has been flooding or rain damage, have an electrician inspect the premises before turning on the breakers.
- G. DON'T connect emergency generators to the building wiring as unsuspecting repair crews may be injured or killed. Operate any necessary equipment directly off the generator. Use generators outside only as they expel carbon monoxide.
- H. Continue to use communication systems only for emergencies.
- I. Remember that water will be contaminated, creating a health hazard.
- J. Employees should be instructed not to attempt to return to work until notified.
- K. Notify outside agencies, such as national or state humane and animal control organizations, of your status. If you need assistance of any kind, the faster you call, the faster it will arrive. It is generally much easier for you to call out of a disaster area than it is for others to call into one.

## **On-Going Planning**

- A. Flood-Plain Map - Keep one posted at all times in employee and public lounges or waiting areas.
- B. Provide regular training for all employees in CPR, First Aid (for humans and animals) and disaster preparations, particularly in tornado, earthquake, and fire response (use of fire extinguishers and their locations in the facility).
- C. Hold quarterly fire, tornado, and earthquake drills.
- D. Review and update your disaster plan annually.
- E. Supplies needed at all times:
  - ▶ Flashlights with batteries (refrigerated for longer life).
  - ▶ Transistor Radio with batteries
  - ▶ Fire Extinguisher
  - ▶ Tarps and/or plastic
  - ▶ Rope or cord

- ▶ Tape
- ▶ Tools necessary to shut down equipment, tanks, etc.
- ▶ First Aid Kits for human and animals
- ▶ Food and water to last for 1 -2 weeks
- ▶ Portable corrals for livestock
- ▶ Collapsible cages or crates
- ▶ Additional collars, leads, leashes, halters
- ▶ Additional office supplies of those items used frequently
- ▶ Weather Alert Radio
- ▶ Police Scanner

F. Make sure personnel are up-to-date on protective shots such as rabies, tetanus, hepatitis, etc.

G. Develop a telephone tree of employees and, possibly, volunteers to notify them of disasters or pending disasters. Make provisions, however, for communication in case telephone lines are down. Pre-arrange meeting sites with needs list in case communication is impossible.

H. Obtain, or get a commitment for, a generator with the capacity to operate basic functions of the facility. If you have obtained a generator for permanent use, have the hook-up to your electric pre-wired by a qualified electrician. Make sure staff know how to properly operate after a disaster.

I. Keep a list of telephone numbers of local, state and national groups that could provide assistance.

J. Develop a communications system with flexibility. Do not depend on one form of communication after a disaster.

- ▶ Telephone tree - those whose telephones are working and who can relay information around and out of the disaster area.
- ▶ Make contacts with local ham radio operators. See if someone can relay messages for the facility after a disaster.
- ▶ Become part of your emergency management department's system.
- ▶ Portable CB's will work short distances if all other systems are down. Information can be relayed by CB until better systems are operating.
- ▶ Cellular phones may not work because of downed relaying towers or crowded airwaves, but are useful to have on hand.

K. Check electrical wiring regularly.

You must also plan for incidents such as tornadoes, earthquakes, or hazardous material releases for which you will have little or no advance warning.

1. Someone should be designated to make the decision on whether to evacuate or stay in the building.



2. If the decision is to remain in the building, safe areas should be identified in advance and employees should be regularly instructed as to the location of the safe areas.

You should also consider the impact of a disaster not just on your facility, but on the neighboring community or region. A disaster in your area may bring a flood of animals to your doorstep, creating a ripple disaster in your shelter.

*Developed by Laura Bevan, The Humane Society of the United States, using information from the "Hurricane Action Guidelines for the Business Community" developed by Sarasota (FL) County Emergency Management.*

# Disaster Plan Quick Check List

This plan developed for: \_\_\_\_\_

Date: \_\_\_\_\_

## I. EVALUATION OF FACILITY

### A. Known dangers to facility in area

\_\_\_\_\_ Storm Surge area

\_\_\_\_\_ Flood Plain

\_\_\_\_\_ Hazardous material plants or disposal sites

\_\_\_\_\_ Railroad tracks

\_\_\_\_\_ Interstates

\_\_\_\_\_ Fuel depots

\_\_\_\_\_ Wildfires

\_\_\_\_\_ Earthquake faults

\_\_\_\_\_ Fire inside facility

\_\_\_\_\_ Heat or cold emergencies

\_\_\_\_\_ Emergency Management has assessed dangers to facility

### B. Dangers of structure

Construction quality of building: \_\_\_\_\_Excellent \_\_\_\_\_Good \_\_\_\_\_Fair \_\_\_\_\_Poor

Glass: \_\_\_\_\_Sliding doors \_\_\_\_\_Large windows \_\_\_\_\_Large number of windows

Kennels: \_\_\_\_\_Indoor / outdoor \_\_\_\_\_Indoor only \_\_\_\_\_Outdoor only \_\_\_\_\_Other

\_\_\_\_\_ Presence of interior "safe" areas

\_\_\_\_\_ Roof hurricane strapped or clipped

\_\_\_\_\_ Exposed, overloaded, or old electrical wiring

\_\_\_\_\_ Professional evaluation of facility

\_\_\_\_\_ Area cleared around structure

## II. INSURANCE

\_\_\_\_\_ Annual check for adequacy

\_\_\_\_\_ Location identified on flood plain map

\_\_\_\_\_ Inventory done

## III. PRIORITIES

\_\_\_\_\_ Identify vital property and protect

\_\_\_\_\_ Movable inventory (i.e. vehicles)

\_\_\_\_\_ Secure furniture

\_\_\_\_\_ Glass secured

\_\_\_\_\_ Fire drill conducted

\_\_\_\_\_ Fire alarm installed

\_\_\_\_\_ Fire extinguishers installed

\_\_\_\_\_ Employees trained to use extinguishers

\_\_\_\_\_ Lightning suppression system installed

\_\_\_\_\_ Adequate hoses attached to building

## IV. EMPLOYEES

\_\_\_\_\_ Pyramid of release

\_\_\_\_\_ Personal disaster plans

\_\_\_\_\_ Non-business hours plan

\_\_\_\_\_ Notification of return

\_\_\_\_\_ Training in C.P.R.

\_\_\_\_\_ Training in First Aid (human & animal)

\_\_\_\_\_ Training in Disaster Planning

\_\_\_\_\_ Cross training done

\_\_\_\_\_ Up-to-date protective shots

## V. SPECIFIC PREPARATIONS

\_\_\_\_\_ Hazardous Materials - Labeled, secured

\_\_\_\_\_ Outside tanks - secured and valves closed

\_\_\_\_\_ Incompatible chemicals separated

\_\_\_\_\_ Update inventories regularly

\_\_\_\_\_ Vital business records protected and secured

\_\_\_\_\_ Prepared for loss of power

\_\_\_\_\_ Outside area clear of loose objects

\_\_\_\_\_ Flags down

\_\_\_\_\_ Refrigerated inventory protected

\_\_\_\_\_ Movable inventory, fueled and protected

\_\_\_\_\_ Freezer emptied of carcasses

\_\_\_\_\_ Generators available

## VI. FINAL SECURING OF PREMISES

\_\_\_\_\_ Contact alarm companies

\_\_\_\_\_ Take identification

\_\_\_\_\_ Unplug equipment, shut off breakers, gas and water

\_\_\_\_\_ Recheck hazardous material valves

## VII. RETURNING AFTER THE DISASTER

\_\_\_\_\_ Rubber gloves and boots

\_\_\_\_\_ Enter with buddy



- \_\_\_\_\_ Flashlights only
- \_\_\_\_\_ Inventory
- \_\_\_\_\_ Safety repairs
- \_\_\_\_\_ Building checked by electrician
- \_\_\_\_\_ Outside agencies notified of status

#### VIII. PLANNING

- \_\_\_\_\_ Flood Plain Map posted
- \_\_\_\_\_ Flashlights with batteries
- \_\_\_\_\_ Transistor radio with batteries
- \_\_\_\_\_ Weather alert radio
- \_\_\_\_\_ Police scanner
- \_\_\_\_\_ Fire Extinguishers
- \_\_\_\_\_ Tarps and/or plastic
- \_\_\_\_\_ Rope and tape
- \_\_\_\_\_ Tools
- \_\_\_\_\_ First Aid Kits (animal & human)
- \_\_\_\_\_ Food/Water
- \_\_\_\_\_ Extra cages and crates, halters
- \_\_\_\_\_ Quarterly disaster drills - test smoke detector batteries
- \_\_\_\_\_ Disaster plan updated annually
- \_\_\_\_\_ Annually recharge fire extinguishers
- \_\_\_\_\_ Identify safe areas from tornados, earthquakes, etc.
- \_\_\_\_\_ Telephone tree created
- \_\_\_\_\_ Electrical wiring checked

On \_\_\_\_\_ this plan should be  
re-evaluated and employees should be re-trained.

\_\_\_\_\_

\_\_\_\_\_  
Signature & Date

# Preparing the Farm and Farm Animals for Disasters

by

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## Introduction

Disasters such as hurricanes, tornadoes, floods, earthquakes, severe winter weather, hazardous material spills or nuclear power plant accidents can occur any time. The event may occur suddenly or be anticipated for several days as with an approaching hurricane or flood. The time to prepare for these events is long before they occur. Even at the farm level, procedures should be written. They should be kept in a safe, fireproof, quickly accessible place with other important documents and taken along if it becomes necessary to evacuate the farm. Each member of the farm family and herd personnel should know of and practice the plan so that action may be taken even in the absence of key management personnel.

The first step in planning for a disaster is to determine what type of disaster could occur on the farm and with what frequency. It would be useless to spend time and money, for example, to plan for severe winter weather if the farm is located in a tropical environment. If the premises are near a nuclear power plant, even though the risk of an accident occurring is slim, the owners would want to consider how to protect their animals from radioactive fallout. If the farm is near a major highway, one might want to consider a hazardous material spill from a road accident in the planning. Living next to a river or stream would put planning for flooding or a barge accident in the forefront.

Only after farm owners have considered their risks can they prioritize the time, money, and other resources they wish to allocate to each potential hazard. An all-hazards plan is most desirable; however, plans should also be customized for specific situations. Once the risks are known, decisions can be made about what actions can be taken in advance and what actions would be required once the disaster occurs. Generally, the effects of a disaster on livestock are lessened by avoiding the disaster, mitigating its effect if it cannot be avoided, or sheltering the animals. The approach taken would depend upon the type of disaster anticipated. Sometimes only one approach may be appropriate such as sheltering. In some instances, combined approaches, such as mitigation and sheltering, may be required. In events such as floods or firestorms, sheltering may be the wrong thing to do.

## Mitigation

Hazard mitigation is defined as any action taken to eliminate or reduce the long-term risk to life and property from natural or technological hazards. Some examples of hazard mitigation might be hurricane seeding to reduce the intensity of a storm, tying down homes or barns with ground anchors to withstand wind damage, redirecting the impact away from a vulnerable location by digging water channels or planting vegetation to absorb water, establishing setback regulations so building is not allowed close to the water's edge, and constructing levees or permanent barriers to control flooding.

The farm and farm buildings should be surveyed to figure out what mitigation procedures should be followed based on the hazard risk. These procedures include:

- building or repairing barns and outbuildings so they exceed building codes;
- constructing or moving buildings to higher ground;
- replacing or covering glass windows and doors with sturdier materials;
- keeping drainage furrows sodded;
- cleaning or moving trash piles and burial sites (Many farms contain burial sites contaminated with lead-based paints, machinery grease, motor oil, lead-lined tanks, batteries, roofing nails, asphalt, shingles, caulking compounds, linoleum and plumbing lead. During flooding this material may leech into the crops or feed supply or be moved to a more accessible area where animals could consume them.);
- moving or storing toxic chemicals, pesticides, herbicides, and rodenticides in secured areas to prevent their washing onto pastures where animals may be exposed;
- securing loose items; and
- draining or building levees around ponds that could flood.

A list of resources and people should be developed by the farmer and kept with important papers. This list should contain emergency phone numbers, suppliers, truckers, and people that can help with the animals, especially if normal working conditions are disrupted.

Supplies that may be needed during or after the disaster should be obtained. Many of these items may not be readily available after the disaster. By obtaining them in advance, more reasonable prices will be paid. Unfortunately, disasters attract individuals who gouge and prey on the misfortunes of victims. Items that could be obtained are portable radios and TV's, extra batteries, flashlights, candles, portable generators, salt, gravel, litter, fuel, antifreeze, stored feed such as hay (the amount to store would depend on the hazard--after the Washington State flood, most producers vowed never to inventory large amounts of hay due to excessive flood damage and spoilage), ropes, halters and other animal restraint equipment, and medical supplies. Once obtained they should be stored in such a manner that they will be usable after the disaster. While in storage they should be checked at regular intervals--i.e., once a week--to assure that they do not spoil, and that electrical or mechanical appliances are still working. They should also be rechecked and evaluated after the event to assure they are still usable. A log should be kept to record when and how often the items were monitored. Animals should be kept current on all appropriate vaccinations and booster shots before the disaster. Keep a written record of the products given and the date of injection. Because the stress of the event and the disruption of the environment could cause an increase in infectious disease spread, proper vaccination could protect the animals.



## **Representation to Governmental Agency Managing the Disaster Response**

As the disaster approaches or after it arrives, the most important thing the farmer needs is truthful, accurate, and current information. Government's response to most disasters is coordinated by a county, State, or Federal emergency management agency. Representation to this agency for the farmer is critical. In most instances, this is competently done by a member of the State or Federal Department of Agriculture. It is strongly suggested that farm organizations lobby for veterinary representation either through their State or Federal Department of Agriculture or separately to the emergency management agency. Often, the needs of animals during disasters are given low priority. Veterinarians, who are aware of these needs and can also verify the validity of requests for help, are most suited to bring animal problems to the forefront. In many instances, actions required to protect animals, such as sheltering or evacuation, must be done before a similar action is taken for people. This is because moving animals to shelter from pasture or evacuating them to other locations takes considerable time and many workers. However, governmental agencies will not issue such directives for animals before similar instructions are issued for people. They fear that a panic situation might occur and people might be critical about animals being protected before them. (Animals can always be released from the shelter or returned from their point of evacuation if the disaster does not materialize.) What they do not consider is that it must be done while it is still safe for people to do the task since animals cannot shelter or evacuate themselves. After the disaster, government usually limits access to the disaster area. However, animals have to be fed, watered, and milked. Who is better suited to do this than the owner? Designation of farmers as emergency workers by government solves the problem of who will be responsible for this task. A veterinarian located in the emergency operating center can get these messages across.

## **Evacuation**

If evacuation of the animals is being considered, then evacuation procedures, places, and routes should be planned. Since all animals may not be able to be evacuated, owners should decide ahead of time which are the most important ones to save. Various decision criteria can be used such as sale value, breeding quality, stage of pregnancy, stage of production, or simply sentimental preference. These animals should be identified ahead of time and a written list kept. If the owner is not home when the disaster threatens, others would then know which animals to save.

Animal evacuation routes must not interfere with human evacuation routes. Alternate routes should be found in case the planned route is not accessible. Places where animals are to be taken should be decided in advance and arrangements made with the owners of these places to accept the animals. Trucks, trailers, and other vehicles should be obtained in advance and the animals acclimated to them so they are not frightened when they have to be used. Restraint equipment, feed and water supplies should be available to use and move with the animals and sufficient people should be on hand to help move them. The animals should be photographed and permanently identified by metal eartag, tattoo, brand, registration papers, or microchip. A permanent record of the identification must be kept as this information is useful in resolving arguments of ownership in case animals gets loose. Papers documenting the identification should be kept with other important papers. Ultimately, the decision to evacuate will depend on the distance to be traveled, the amount of time before the disaster will affect the farm, and whether there is any advantage to moving the animals to the place selected. Sometimes evacuation may be done after the disaster, provided the roads are passable and the equipment needed for travel usable. If this is the case, the accepting location must be contacted to find out its condition.

## **Sheltering**

Whether to move farm animals to shelter or leave them outside will depend on the integrity and location of the shelter being used and the type of disaster. During Hurricane Andrew, some horses left outside suffered less injury than those placed in shelters. This was because some shelters selected did not withstand the high winds. Horses were injured by collapsing structures and flying objects that may have been avoided on the outside. Another reason for possibly leaving animals unsheltered is because flood waters that inundate a barn could trap animals inside, causing them to drown. During severe winter weather, shelter animals from icy wind, rain, and snow. Generally, if the structure is sound, the animals should be placed indoors. Once they are inside, secure all openings to the outside. As mentioned previously, the sheltering should be ordered and completed before similar action is taken for humans.

Farm cats and dogs should either be placed in a disaster-proof place or turned loose, as they generally will stay close to their home in the immediate period following a disaster. If they are loose, however, attempts must be made to immediately catch them after the threat is over to prevent these animals from becoming feral and a public health hazard. Some farm dogs are dangerously aggressive, and under normal circumstances should be kept chained. These dogs cannot be kept chained or turned loose during a disaster. If an inside shelter cannot be found, then the only safe and humane thing to do is to euthanize these dogs as a last measure before evacuation.

## **Human evacuation**

What can be done with the animals if there is a need to evacuate the premises and the animals have to be left unattended? There is always the risk that animals left unattended for extended periods could die or suffer injury. Sometimes, this may be the only option to protect human life. Protecting human life should always take priority in planning. Regardless, after the animals are secured in appropriate shelters, food and water should be left for them. The amount necessary for survival is considerably less than for other purposes. If the animals survive, then the decision can be made after the disaster whether it is worth the time and expense to bring them back to their previous condition.

Consult the table as a guide to the amount of food and water to leave. Every practical effort should be made to leave animals with sufficient food and water for their survival--enough for 48 hours should be left. Usually, within that time the initial effects of the disaster will be over. During the recovery phase, the decision can then be made as to the best way to mount a rescue effort.

## **Special Considerations**

Some practices that may be followed in planning for disasters, especially during the winter, require a special alert. During winter weather it is common to use portable heaters, gritty substances on the floor to prevent slipping, and antifreeze. When using these heaters, be sure they are working properly and are located in an area where there is adequate ventilation. Heaters not working correctly could be a source of carbon monoxide, a deadly, odorless, colorless gas. Antifreeze used in vehicles is a deadly poison. Animals seem attracted to it and will readily consume it because of its sweet taste. Take care to properly label all containers. Do not use containers previously filled with antifreeze for other purposes, especially feed and water. Promptly clean up all leaks and spills. Water supplies should be checked for freezing. Many animals have died of thirst during the winter, even with abundant water sources, because they could not drink the water as it was frozen solid. If

gritty material is spread on floors to prevent slipping, use only approved nontoxic materials. Recently, a farmer mistakenly used Furadan, a fungicide, for this purpose and several cows who licked it off the floor died.

Farms can be insured against catastrophic events. Insurance policies are available for replacement of damaged materials, repair work for recovery, boarding of evacuated occupants and animals, lost production, and relocation. These should be investigated and purchased before the disaster threatens. For a farmer to claim compensation for lost production, which in many cases is the largest economic cost during a disaster, the farmer must have substantial records that document the level of production his/her herd has achieved in previous years. This is generally only successful in herds with recognized herd monitoring programs, such as Dairy Herd Improvement or other programs that are available for various species. To verify the validity of these records a herd health program, based on a valid veterinarian-client-animal relationship, should be in place. A copy of all production records should be kept in a secure place so that the details are not lost during the disaster. Many veterinarians are willing to keep copies of their clients' production records, if they are computerized and space efficient.

## **Conclusion**

Depending upon the event, disaster preparation may or may not be successful. However, it is known that effects of disasters are lessened by proper planning. Economically, it is cheaper to prevent the problem or lessen its effect than to pay the costs of recovery. The time to do this is NOW, before the disaster occurs.

<b>ANIMALS</b>	<b>WATER/DAY</b>	<b>FEED/DAY</b>
<b>DAIRY COWS</b>		
IN PRODUCTION	9 GALLONS SUMMER	20 POUNDS HAY
	7 GALLONS WINTER	
DRY COWS	9 GALLONS SUMMER	20 POUNDS HAY
	7 GALLONS WINTER	
WEANING COWS	6 GALLONS SUMMER	8-12 POUNDS HAY
	3 GALLONS WINTER	
PREGNANT	7 GALLONS SUMMER	10-15 POUNDS LEGUME HAY
	6 GALLONS WINTER	
COW WITH CALF	9 GALLONS SUMMER	12-18 POUNDS LEGUME HAY
	8 GALLONS WINTER	
CALF (400 POUNDS)	6 GALLONS SUMMER	8-12 POUNDS LEGUME HAY
	4 GALLONS WINTER	



<b>ANIMALS</b>	<b>WATER/DAY</b>	<b>FEED/DAY</b>
<b>SWINE</b>		
BROOD SOW WITH LITTER	4 GALLONS SUMMER	8 POUNDS GRAIN
	3 GALLONS WINTER	
BROOD SOW (PREGNANT)	1-2 GALLONS SUMMER	2 POUNDS GRAIN
	1 GALLON WINTER	
150 POUND GILT OR BOAR	1 GALLON	3 POUNDS GRAIN
<b>SHEEP</b>		
EWE WITH LAMB	1 GALLON	5 POUNDS HAY
EWE, DRY	3 QUARTS	3 POUNDS HAY
WEANING LAMB	2 QUARTS	3 POUNDS HAY
<b>POULTRY</b>		
LAYERS	5 GALLONS/100 BIRDS	17 POUNDS/100 BIRDS
BROILERS	5 GALLONS/100 BIRDS	10 POUNDS/100 BIRDS
TURKEYS	12 GALLONS/100 BIRDS	40 POUNDS/100 BIRDS
<b>HORSES</b>		
ALL BREEDS	5 GALLONS/1000 POUNDS	20 POUNDS HAY/1000 POUNDS
<b>DOGS AND CATS</b>		
ALL BREEDS	1 QUART/DAY/ANIMAL	AD LIBITUM DRY FOOD

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Descriptors: overview of emergency services in California, guide to roadblocks and fire designations, standardized emergency management system, articles, training manuals, workshops, videotapes and other information resources, disaster planning—a comprehensive look at developing a response program, contacts in California, emergency contacts in California—includes animal transporters, animal shelters, feed and supply stores, pet stores, veterinary personnel, sample animal care guidelines and forms.

Vogelweid, C.M. (1998). **Developing emergency management plans for university laboratory animal programs and facilities.** *Contemporary Topics in Laboratory Animal Science* 37(5): 52-56.

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Descriptors: creating your plan, establish a planning team and obtain authorization to develop the plan, analyzing response capabilities and identifying specific hazards that are likely to effect an animal facility, develop your plan, include proper authorities—fire, police, environmental safety, community outreach, recovery and restoration of services, implementing the plan, training, .

## Useful World Wide Web Sites

### **American Red Cross Disaster Services**

<http://www.redcross.org/disaster/safety/guide.html>

The mission of American Red Cross Disaster Services is to ensure nationwide disaster planning, preparedness, community disaster education, mitigation, and response that will provide the American people with quality services delivered in a uniform, consistent, and responsive manner.

### **Federal Emergency Management Agency (FEMA) Virtual Library and Electronic Reading Room**

<http://www.fema.gov/library/lib07.htm>

Pertinent resources include full-text documents in the following categories:

*Animals in Emergencies*

*Preparedness, training, and exercises*

### ***Response and recovery***

#### ***U.S. Fire Administration***

The online library of FEMA contains full-text resources for planning your disaster response program. Also includes information in Spanish. An excellent resource provided by the Federal Government.

#### **Florida Animal Disaster Planning Advisory Committee**

<http://www.fl-adpac.org/>

ADPAC is an ad hoc group of organizations and individuals interested in promoting the effective development and implementation of disaster plans to protect animals.

#### **University of Colorado Health Sciences Center Animal Care & Use Program**

<http://www.uchsc.edu/sm/animal/index.html>

This document is designed to do the following: Guide you during emergencies; Inform you of potential emergency situations before an emergency occurs; and Help you to avoid and anticipate dangerous situations To access this site, scroll down the left frame and click on After Hours Emergencies/ Disaster Prep.

#### **University of Florida Emergencies**

<http://nersp.nerdc.ufl.edu/~iacuc/Emergency.htm>

The Animal Resources Branch is responsible for emergency planning and implementation with regard to the research animals. This manual will serve as an annex to the University of Florida Natural Disaster/Hurricane Emergency Plan in addition to other Emergency Procedures (i.e. fire, flood, threats by animal activists, etc.) as established by the University of Florida.

#### **University of Florida Institute of Food and Agricultural Sciences and the Florida Cooperative Extension Service**

<http://disaster.ifas.ufl.edu/>

The Disaster Handbook Web site is one component of the Comprehensive Disaster Preparedness and Recovery Education Module, which also includes: The Disaster Handbook (Print and CD-ROM Editions) and "Are You Ready?" a video based on the Disaster Preparedness Satellite Video conference.





# **Animal Welfare Laws, Legislation, and Regulations**

**A Brief Literature Review**





# Thirty Years of the Animal Welfare Act

Congressman George E. Brown, Jr.

*The author represents the 42nd District of California and has been instrumental in passage of animal welfare legislation in the U.S. Congress. This article is taken from a speech prepared by Congressman Brown in September 1996 commemorating the 30th anniversary of the Animal Welfare Act.*

[Editor's note: Congressman Brown died on July 15, 1999.]

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I appreciate the opportunity to be with you today to celebrate the 30th anniversary of the Animal Welfare Act. The Animal Welfare Act is this Nation's primary Federal law regarding animal care, and it sets standards for the treatment of animals by breeders, exhibitors, and transporters, as well as research facilities using animals in research. The passage of the Animal Welfare Act was a monumental achievement, and it has been improved upon through subsequent amendments. However, all of us who work on these issues know that more still needs to be done in the next 30 years.

Advocates of a humane ethic for animals are gaining momentum in this country. This movement gains its strength from a very basic philosophy regarding the sacredness of life. While recognizing the role that animals have traditionally played in society as food sources, companions, and research models, we have to always remember that animals are sensing, living beings capable of feeling fear and pain, and that they must be respected as such.

There are few issues confronting Congress where the advocates hold such an emotional commitment. Promoting proper care and protection of animals has been a priority of mine throughout my public career. Several issues were being brought before the California State Legislature when I was a representative close to 40 years ago. And to be quite frank, these issues are, more often than not, low on the overall political agenda of our policymakers and are not regarded as the most critical issues of the times.

As you know, politicians are fairly slow to propose controversial changes. To be too far in the forefront of our changing culture is to commit political suicide. Because of the lack of political motivation and the unfortunate opposition which many times accompanies efforts to improve the treatment of animals, changes made regarding animal welfare laws have been gradual changes over time, designed to keep abreast, or at least to minimally address, changing views in our society. The Animal Welfare Act and the subsequent amendments, therefore, represent important, but moderate changes, made in response to the growing concern about the welfare of animals.

In October 1981, we held hearings in the Science Subcommittee reviewing current practices of laboratory animal care, use, and treatment. The 2 days of public hearings centered on testimony by representatives from Federal agencies, animal welfare societies, and research and educational institutions.



The hearings were a result of an individual's claims to police a month before and the subsequent arrest of a researcher and his animal caretaker on charges that 17 monkeys were being mistreated at a Silver Spring, Maryland, research facility.

The subcommittee's review also provided grounds for additional congressional hearings that focused on the Animal Welfare Act. Senator Bob Dole conducted hearings in 1983, and I held hearings in 1984. The testimony presented at those hearings was, by and large, the basis for legislation that we sponsored in 1984 and 1985—the “Improved Standards for Laboratory Animals Act.” The purpose of the legislation was to amend some provisions of the Animal Welfare Act (AWA) in light of allegations that the U.S. Department of Agriculture was not adequately enforcing the standards established for the care and treatment of laboratory animals.

This legislation addressed the legitimate concerns which arose from well-publicized accounts of substandard research facilities which had neglected animals and grossly violated animal care regulations. It was basically another step to bring our laws a little closer to the growing concern about the care of laboratory animals. At the same time, the legislation was moderate and did not place an unbearable burden upon research institutions.

The 1985 amendments strengthened standards of animal care by requiring the use of pain killers and presurgical and postsurgical care, requiring animal care training for personnel who work with animals, requiring euthanasia of an animal upon completion of an experiment, and provided for exercise of dogs and a physical environment to promote the psychological well-being of nonhuman primates. The amendments also required the Animal and Plant Health Inspection Service (APHIS) to inspect facilities at least once a year and to inspect Federal agencies' facilities. It also established a national information service [the Animal Welfare Information Center] on alternative research procedures, as well as on ways to reduce unintended duplication of experiments.

Ideally, it would be nice if we could develop sufficient alternative procedures to be able to eliminate the use of live animals altogether, through the use of tissue cultures, computer programs, and other models. I strongly support the development of alternatives to the use of live animals wherever possible. While Chairman of the Subcommittee on Science, Research, and Technology, I held hearings on the use of animals in research and on alternative research methods. In this subcommittee, I had the opportunity to work on legislation providing for the humane care of laboratory animals and which encouraged the development of alternatives to the use of live animals in research.

In addition to the issue of the care and treatment of animals, the problem of lost or stolen companion animals being used for research was also a major motivation for the original enactment of the Animal Welfare Act.

Unfortunately, the Animal Welfare Act has not had great success in preventing lost or stolen pets from entering the research animal trade. This is mainly because the statute allows individuals who gather animals from random sources to be licensed by the USDA to provide these animals to research facilities. These dealers, known as Class B dealers, routinely buy and sell stolen family pets, purchase animals without records from public auctions, and “adopt” animals from pounds and families under false pretenses.

For many years, I have been deeply concerned that the pet theft provisions of the Animal Welfare Act are not being adequately enforced. It has been revealed, through the media and through USDA's own Inspector General, that inspectors have knowingly ignored repeated violations of Federal laws, including the falsification of records of animal origins, the only way to ensure that stolen animals are not entering the research animal trade.

As Chairman of the Department [of Agriculture] Operations, Resources, and Foreign Agriculture Subcommittee, I held a hearing on the Pet Theft Act during the 100th Congress. This measure was designed to protect household pets from being stolen and sold to research laboratories. This legislation had passed the Senate but failed to reach the House floor before Congress adjourned.

In April of this year [1996] I joined Congressman Charles Canady in introducing H.R. 3398, the Pet Safety and Protection Act, which would amend the Animal Welfare Act to ensure that all dogs and cats used by research facilities are obtained legally.

Adequately addressing the problem of pet theft is one of many challenges that APHIS and the Animal Welfare Act will face in the coming years. In the areas of animal care and treatment, the Animal Welfare Act needs to be strengthened and improved upon. This may require USDA coming to Congress and requesting legislation that will grant them greater authority to effectively enforce the Act.

The USDA Inspector General's January 1995 report—Animal and Plant Health Inspection Service (APHIS) Enforcement of the Animal Welfare Act—stated, “APHIS does not have the authority ... to effectively enforce the requirements of the Animal Welfare Act.” I am deeply concerned with the agency's ability and willingness to adequately monitor and reasonably ensure the humane care and treatment of animals.

Lack of adequate resources is part of the problem associated with APHIS' ability to adequately monitor and inspect animals and facilities and to enforce the pet theft provisions of the Animal Welfare Act. In the past, I have testified before the Appropriations Committee in favor of increased funding for enforcement of the AWA. Members of Congress concerned about the funding levels for APHIS had to be particularly diligent during the Reagan Administration, when repeated attempts were made to eliminate entirely funds to enforce the Animal Welfare Act.

In addition to fiscal constraints, however, the Inspector General's report indicates that APHIS has been neglecting its statutory obligations and has renewed facility licenses even when cited violations—past and present—had not yet been corrected. Additionally, APHIS is not inspecting research facilities before issuing the initial registrations; therefore, noncompliance with the Act may go unnoticed until APHIS' first inspection up to a year later.

It was clearly the intent of Congress that facilities should come into compliance before being issued the initial registrations. Section 2.3 of the Animal Welfare Act, among others, implicitly gives APHIS the authority to conduct inspections and to deny renewals.

I hope that the advances made through the Animal Welfare Act and other legislation aimed at protecting animals can be improved upon in future years. Much more needs to be done to ensure that the animals in our care are treated humanely. This should not be seen as a threat to the research community. It is simply a reaction to the growing concerns of society and should be accepted as

such. And it is in the best interest of those who rely on animals to accept this growing change and work with policymakers to develop legislation which addresses the concerns of the animal welfare movement while, at the same time, developing regulations which do not cause unreasonable burdens.

A large portion of Americans feel strongly that animal care laws are important and should be enforced. The Animal Welfare Act has provided a baseline of humane care that is necessary and just. I am hopeful that we can move forward from here and provide a more meaningful level of protection for the thousands of animals under the current jurisdiction of APHIS. I look forward to seeing us move forward into the next 30 years of the Animal Welfare Act building on past successes and with a progressive approach toward rectifying the remaining problems associated with the enforcement of the Act.



# Validation of *in Vitro* Methods: Regulatory Issues

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## Introduction

The U.S. Food and Drug Administration (FDA) is primarily concerned with public safety. To that end, the use of animals in toxicity testing has played an important role in hazard/safety determination for regulated products. FDA encourages the development of alternative methods to animal testing (e.g., *in vitro* tests) and is aware that many such tests are in various stages of evolution. New laws have been enacted that either ban the use of animals in testing for certain products or mandate the development and validation of alternative methods to animal testing. Research has resulted in much activity in the development of *in vitro* methods intended for use as screens, adjuncts, and replacements for current *in vivo* standards. For example, although technical progress in the development of non-whole animal testing methods has occurred, to date, no single test, or battery of tests, has been accepted by the scientific community as a replacement to the animal model currently used in ocular irritation testing, the Draize test. For replacement of the *in vivo* standard with *in vitro* tests, further research is needed to better understand the mechanisms of action of ocular irritants *in vivo*. Criteria for the validation and acceptance of *in vitro* methodologies intended to replace *in vivo* models need to be well defined; moreover, new risk assessment paradigms to analyze information generated by *in vitro* methods need to be developed. The international community should strive for harmonization based upon consistent, science-based standards, while pursuing improved methods intended to protect public health worldwide.

## The FDA Mission

The mission of the FDA is to assure the American consumer that foods are pure and wholesome, safe to eat and produced under sanitary conditions; that drugs, medical devices, and cosmetics are safe and made from appropriate ingredients; and that labeling and packaging for these products are truthful and not deceptive. The authority for this mission is issued under the following laws: 1) Federal Food, Drug, and Cosmetic Act (FFDCA) (21 U.S.C. 301-392) and its accompanying regulations and the Fair Packaging and Labeling Act (FPLA) (15 U.S.C. 1451-1461), which apply to foods and drugs for humans or animals, cosmetics, and medical devices; 2) Sections of the Public Health Service Act (PHSA) relating to biological products for human use (42 U.S.C. 262-263) and control of communicable diseases (42 U.S.C. 264); and 3) The Radiation Control for Health and Safety Act, relating to electronic products which emit radiation, such as x rays, lasers, microwave ovens, and TV sets (42 U.S.C. 263b-263n).

## Drugs, Cosmetics, and Devices Defined

A drug is an article intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in humans and other animals and articles (other than food) intended to affect the structure or any function of the body of humans or other animals. It is the intended use which



determines whether an article is a drug; therefore, foods and cosmetics may also be subject to the drug requirements of the law if therapeutic claims are made for them. The FFDCA defines cosmetics as articles intended to be applied to the human body for cleansing, beautifying, promoting attractiveness, or altering the appearance without affecting the body's structural function. A device is defined as any health care product that does not achieve any of its principal intended purposes by chemical action in or on the body or by being metabolized. The term "devices" also includes components, parts, or accessories of devices, diagnostic aids such as reagents, antibiotic sensitivity discs, and test kits for *in vitro* diagnosis of disease and other conditions (1).

## **Regulations and Animal Use**

The FFDCA and the PHSA require manufacturers of certain consumer products to establish, before marketing, that such products meet the safety and effectiveness requirements of the law and are properly labeled. FDA regulations prescribe the type and extent of premarket testing that must be conducted, depending on the legal requirements applicable to the particular product and on the technology available to fulfill those requirements. Testing may include physical and chemical studies, non-clinical laboratory studies, and clinical tests.

Animal tests are required by FDA for drug products, vaccines, certain medical devices and electronic products, food and color additives, and new animal drugs. "Although the FFDCA does not require that cosmetic manufacturers or marketers test their products for safety, the FDA strongly urges cosmetic manufacturers to conduct whatever toxicological or other tests are appropriate to substantiate the safety of the cosmetics (2)." These tests should be state-of-the-art and generally represent consensus of the scientific community.

## **Regulation of Cosmetics vs. Drugs and Medical Devices**

Cosmetics marketed in the United States, whether made here or imported, must comply with the FFDCA, the FPLA, and regulations issued under the authority of these laws. Unlike those products regulated by FDA that require premarket review prior to approval, there is no requirement for or against the use of animals in the substantiation of safety of the methods used by cosmetic manufacturers in testing their products. Ordinarily, a cosmetic comes under scrutiny only if a problem surfaces post-marketing. For example, if a product causes injury, such as severe ocular or dermal irritation or is otherwise shown to be deleterious to public health, the agency can require its withdrawal from the market. There appears to be a trend away from the use of animals in cosmetic testing, as many manufacturers join a growing group of those who claim to no longer use the animal model.

The application process for approval of human drugs may incorporate both *in vivo* and *in vitro* methods for toxicity testing; however, to determine efficacy or substantiate safety for products intended for use in humans, clinical trials are required for final approval of drugs and devices. Although not a regulatory requirement, the final product formulation in cosmetic testing is usually not marketed to the public until some form of limited human testing has occurred. The fundamental issue is that hazard determination and safety substantiation, although inextricably linked, are not the same. Safety is a relative concept and is achieved through a process of elimination. After all the evidence is considered, a decision is made based upon benefits of the proposed product compared to its risks.

## Methods for Hazard/Safety Determination

For approximately 50 years, the rabbit has served as the model for eye and skin irritation testing (*viz.*, the Draize tests). To date, salient issues have centered around “replacement” of the Draize eye and skin tests with *in vitro* methods. Unlike drugs and medical devices, where the product may not be marketed without regulatory approval, cosmetics are presumed substantiated for safety before marketing. If this is not the case, then the sponsor of the product must communicate this fact by placing a warning statement on the label. Since a warning statement on a cosmetic label is exceedingly rare, and most likely non-existent, the consumer regards cosmetics marketed in the United States as safe. *In vitro* methods play a significant role in the toxicological evaluation of raw chemicals, therapeutic drugs, medical devices, biologicals, and cosmetics; their current application is that of screening for toxicity, especially for moderate to severe irritants, primarily as a component of a tiered testing system that seems to differ considerably “in house” depending upon the company or government to whom one may speak.

## Current Utility of *In Vitro* Methods

The use of *in vitro* methods as part of different ocular irritancy testing systems was recently demonstrated in a workshop organized by the Interagency Regulatory Alternatives Group (IRAG) titled “Workshop on Eye Irritation Testing: Practical Applications of Non-Whole Animal Alternatives.” Two hundred people participated in the workshop where approximately 40 laboratories from around the world submitted 55 data sets representing 23 *in vitro* methods. Expert working groups were formed to review each of the major assay systems, and their summaries were presented during the workshop. While several salient topics relevant to the status of non-whole animal methods development and use were addressed during this workshop, a significant message was clear: many companies and some governments have established alternative testing systems to help evaluate certain chemicals and products for ocular irritation potential, and *in vitro* methods are an important part of those processes.

## *In Vitro* Testing Methods and Regulatory Acceptance

Certain external influences (3,4) are driving change that will most likely result in *in vitro* methodologies occupying a more prominent place in toxicity testing. The cosmetic industry, in particular, is looking to Federal agencies for guidelines identifying regulatory acceptance criteria for submitting data generated from *in vitro* methods intended to at least partially replace some data that, heretofore, originated from *in vivo* testing. Although specific criteria for regulatory acceptance of *in vitro* models have not yet been published, validation of a proposed model may be considered an important criterion in this process.

Although validation of new methods is not a primary responsibility for regulatory agencies, validation by the scientific community may be considered pivotal to regulatory acceptance. However, “validation” of a method does not necessarily guarantee regulatory acceptance. Like pre-market approval of regulated products, the acceptance criteria of a proposed new method will largely be determined by the sponsor's claim for the test. As part of the review of a proposed *in vitro* method during the risk assessment process, new data need to be evaluated, and herein lies a formidable challenge; *viz.*, new standards of data comparison need to be considered.

When an *in vitro* method is proposed to test for an *in vivo* response, such as dermal or ocular irritation, the qualitative data generated by the test as compared to the *in vivo* standard are imperative. In other words, what are the endpoints and how do they relate to the tissues evaluated by the Draize. For example, discussion often centers around the empirical vs. mechanistic approach. A correlative (empirical) method, which may successfully identify a severe dermal or ocular irritant early in the evaluative stages of testing, may be acceptable to the regulatory agency as a screen, but since it does not predict safety, would be inadequate as a replacement. However, for a method to successfully identify a severe irritant with an acceptable level of false positives (substantiate hazard/high sensitivity) and predict safety with a low incidence of false negatives (substantiate safety/high specificity), a full understanding of the mechanism by which the technique detects irritation in a specific tissue appears to be essential to replacement (3).

### ***In Vivo* "Replacement"**

What, then, needs to be accomplished by the scientific community to advance the acceptance of new techniques? For true replacement of an *in vivo* with an *in vitro* model to successfully occur, research should focus on the mechanisms of dermal or ocular irritation in humans. It appears, therefore, that methods development targeted for replacement will need to successfully predict the presence or absence of irritation at the physiological, anatomical, biochemical, or molecular level of tissue pathology. Tissue repair, the reversibility of lesions, is an important facet in classification of substances; moreover, in the review of FDA-regulated substances, those products that cause irreversible damage to some tissues would be less likely to receive approval. Similarly, some products may not cause severe tissue damage or visible irritation upon exposure but may cause considerable discomfort or pain. Demonstrating such phenomena will be most difficult without *in vivo* modeling. These examples highlight formidable challenges that need to be addressed as issues germane to total replacement are identified and explored.

As we try to envision replacement of the animal model in the context of safety substantiation, several considerations clearly need to be addressed. Few would accept the simplistic notion of total replacement of an animal model, such as the Draize, with a single *in vitro* test. A risk assessment system that replaces an animal model will necessarily consist of a multidisciplinary approach that incorporates information from several sources in a systematic or tiered approach.

### **The Tiered Approach to Substance Testing**

The first level will be that of reviewing information already known about the particular class in which the substance resides. It is important to note here that much of the historical information is derived from *in vivo* testing such as dose response relationships as well as toxicokinetic and toxicodynamic data. Other sources include structure activity relationships and known physical-chemical properties of the class from which the substance is derived. The next tier in the system may consist of a battery of assays, each measuring various mechanisms of dermal or ocular irritation. Finally, a decision point is reached; if there is sufficient evidence that the substance is a severe irritant, it may be classified. If insufficient information exists to classify, then further *in vivo* data are required. As methods are examined for their role in irritation testing, a standardized validation paradigm must be developed. A framework for such a model was reported in ATLA (6) from the CAAT (7)/ERGATT (8) Workshop and proposed by the Johns Hopkins University Center for Alternatives to Animal Testing (9).



## Components of Methods Evaluation

As a validation paradigm is considered, the protocol and the data generated by the study are of particular importance for serious evaluation. The protocol for an *in vitro* method should clearly identify the *in vivo* endpoints, and the data generated from the test should provide information relevant to these endpoints. Once *in vitro* data have been accumulated, the standard to which they will be compared is extremely important. To that end, careful consideration must be given to the guidelines established for *in vitro-in vivo* data comparisons. Currently, this is established on a case-by-case basis with FDA-regulated products. Until a model for risk assessment based upon *in vitro* data is developed, there must be adequate means of comparing the results of our tests with known *in vivo* outcomes.

From a regulatory perspective, the following precepts should be considered as guidelines of the scientific process for validation testing of proposed methodologies:

- Define the mechanistic relevance of the *in vitro* test endpoint to effects observed *in vivo*.
- Determine the relationship between the known *in vivo* dermal or ocular irritation potential of the test substance and the *in vitro* test results.
- Demonstrate the quality of the *in vitro* data by evaluating the method's protocol, intra-laboratory repeatability, inter-laboratory reproducibility, number and type of chemicals used, and adherence to GLP (10) standards.
- Define potential uses and limitations of the alternative method including type or class of chemical to which it has application and how the data might be used for practical safety or hazard determinations (11).
- For new molecular entities with no history of previous testing, animal data will have to validate any *in vitro* testing system for that class of compounds.

The following expands upon nomenclature germane to new methods development, validation, and regulatory acceptance:

- *Sensitivity* is the ability of the proposed method to detect that proportion of those compounds tested that are truly positive as an irritant or toxicant. Although a high sensitivity is important in any risk assessment scheme, false positives in sensitivity testing error toward the conservative and, therefore, do not present the unfavorable consequences that may occur with false negatives in specificity testing.
- *Specificity* is the ability of the proposed method to detect those compounds tested that are truly negative as an irritant or toxicant. False negatives in specificity testing mean truly positive substances fail to be detected, thus, allowing a potential toxicant to be classified incorrectly and inadvertently allowed for human/animal use. Clearly, a high specificity is extremely important from a regulatory perspective.
- *Predictive Value* in screening tests is the probability that a positive test is truly positive and a negative test is truly negative.
- *Precision* is the quality of being sharply defined or stated (e.g., the number of distinguishable alternatives from which a measurement was selected). An example of precision would be the standard deviation or comparing the standard deviation to the mean or the coefficient of variation (12).



- *Repeatability* is the ability of the results of a testing method to perform consistently when conducted several times within a particular laboratory. The standard deviation may be employed as a measurement of precision when considering repeatability.
- *Ruggedness* or *rigor* refers to the method's ability to achieve a suitable degree of repeatability in the sponsor's laboratory. Without ruggedness or rigor, a method would not be expected to perform adequately in different laboratories.
- *Reproducibility* is the ability of the results of a testing method to perform consistently when conducted in different laboratory settings. The standard deviation may be employed as a measurement of precision when considering reproducibility.
- *Bias* is the deviation of results or inferences from the truth or processes leading to such deviation. Bias may occur when any trend in the collection, analysis, interpretation, publication, or review of the data leads to conclusions that are systematically different from the truth. There are many sources of bias including flawed study design, data collection, statistical summary data, data analysis or interpretation, instrumental error, handling of outliers, and prejudice in study procedures that lead to one-sidedness in any facet of a study (13).

## Summary

Many challenges face stakeholders now and in the future for risk assessment in the area of toxicity testing. The notion of replacement will vary considerably depending upon many variables. Particularly cogent at this time is the need to identify criteria for both the comparison of *in vitro* with *in vivo* data and regulatory acceptance for *in vitro* methods intended to replace the animal model in toxicity testing. The transition from comparing *in vitro* data to the animal standard to that of a "Gold Standard" is complex and will require the implementation of a novel risk assessment paradigm. Validation of *in vitro* methods needs to adhere to the scientific precepts of purpose and endpoint identification, correlative vs. mechanistic basis, intralaboratory reproducibility, interlaboratory repeatability, protocol standardization, technology transfer, chemical reference standardization, data base development and quality control/quality assessment through GLP-like standards. Finally, this necessarily requires an international effort to coordinate and harmonize the multifaceted issues in risk assessment for hazard/safety determination.

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NAL Call number: SF781 R4

AB- The author outlines the regulation of animal experimentation in the United States of America (USA). Regulation in this field is at the developmental stage; issues are still being defined as public interest in animal welfare focuses on various aspects of animal science. Society continues to initiate regulations for animal experimentation in response to technological advances which were unknown when the first USA Federal legislation in this field (the Laboratory Animal Welfare Act) was signed in 1966. Under the sponsorship of animal welfare activists and, more recently, animal rights advocates, amendments to the 1966 law have increased the scope of Federal authority by extending both the number of species covered and the areas of care which are regulated. A greater awareness has evolved of the issues raised by animal experimentation, both among the general public and within the scientific communities. The importance of the Institutional Animal and Care Use Committees in research facilities is described, together with other factors which affect Federal legislation. Government regulatory philosophy is also changing towards a participatory relationship between regulators and public interest groups. Various affiliations to global and regional organizations have heightened national awareness with regard to the perceived exploitation of animal species. The author demonstrates clearly that the prevailing trend in the USA is towards expanded agreements which are jointly derived and implemented, and which will be instrumental in the search for resolutions. The author concludes that these resolutions will continue to revolve around the ethical need to respect the nature of animal species and the need for knowledge concerning both humans and animals which can help to extend and enhance the quality of life.

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NAL call number: 410.9 P94

Descriptors: laboratory animals, animal welfare, legislation.

## Useful World Wide Web Sites

### APHIS Press Releases

<http://www.aphis.usda.gov/lpa/press/press.html>

Press releases on APHIS programs are prepared by Legislative and Public Affairs (LPA) writers within APHIS and are issued to the media nationally by the Department and regionally or to specialized audiences by APHIS.

### Lab Animal, Regulation Watch

<http://www.labanimal.com/col/col.htm>

A monthly column devoted to animal-related regulatory activities.

# **International Perspectives**







# Regulation of Animal Research in Selected European Countries

*The following information is generously provided by the European Biomedical Research Association. Their website may be accessed at <http://www.ebra.org>*

## Animal Experimentation Legislation in The Netherlands



Under the Dutch Animal Experimentation Act (1977) the heads of research establishments can apply to the Ministry of Welfare, Public Health and Cultural Affairs to be issued with a licence to perform animal experiments. When applying for such a licence, they must specify what type of animal research will be conducted in the institution, but there is no specific control of individual research projects involving animals. The Ministry must normally give a decision on the application within two months and a notice about the licence, the purposes of the experiments and the conditions applied to them is published in the Netherlands Government Gazette. There is no specific limit to the duration of a licence.

Each institution is required to appoint a veterinary surgeon or other qualified expert in animal welfare who is responsible for supervising the welfare of the laboratory animals. In addition this person has wide powers to check that the provisions of this Act are being correctly observed. They make an annual report to the licence holder and to the Chief Veterinary Inspector.

The person responsible for determining the way that an animal experiment is performed must hold a doctoral degree in biology, medicine, veterinary medicine or dentistry and to have completed a specified course on laboratory animal science. There are specific requirements for the expertise and training of persons conducting animal experiments or looking after the animals, the size and construction of cages, the cleaning and heating of animal houses and the feeding of the animals.

Laboratory animals have to be obtained from a licensed animal breeder or animal research institution. They must be housed and cared for and handled so as to satisfy, as far as possible, their physiological and ethological needs. No animal experiment can be conducted for a purpose which, according to a consensus of expert opinion, could be achieved without using animals. No experiment can be conducted on a monkey, dog, cat or horse if another species would suffice. Anesthetics are required where the animals might otherwise suffer appreciable pain, unless these would defeat the object of the experiment. Detailed records must be kept of all the animal experiments conducted.

The legislation instituted an Animal Experiments Advisory Committee, composed of experts on animal research and animal welfare, which is consulted about any general administrative orders concerning animal husbandry, record-keeping, training, etc. In addition, the committee may offer advice of its own volition.

The enforcement of the Act is the responsibility of the Veterinary Public Health Inspectorate, which has an Animal Experimentation Department of six staff. They can enter any animal research

premises, take samples, examine animals and require researchers to provide information or copies of records. Any misdemeanors have to be reported to the public prosecutor. This legislation is currently being amended. The main change which the amendments will introduce will be a requirement for local animal ethics committees, including external lay representatives, at each animal research institution. The exact role and powers of these committees is not yet known.

## **New legislation in The Netherlands**

On 5 February 1997, a revised Experiments on Animals Act came into force in the Netherlands. The original Act, dating from 1977, was reviewed in the EBRA Bulletin in July 1995 (see above).

Under that legislation, the Ministry of Welfare, Public Health and Cultural Affairs could grant a licence to the head of a scientific institution on the basis of an application describing the type of animal experimentation to be performed. However, there was no external control of individual research projects. Each institution had to appoint an animal welfare officer to supervise the well-being of the animals. In addition, the person responsible for determining the way in which an animal experiment was performed had to hold a doctoral degree in a relevant subject. The law also contained other provisions based on the EU Directive 86/609.

The main change introduced by the revised Act is to require that research plans must be approved by an ethical review committee, which has to consider the benefit to come from the experiments and whether this justifies the distress caused to the animals to be used. No maximum duration for a research plan is stipulated. Committees are required to give a decision on an application within three months and, if they do not approve the research plan, the applicant can appeal to the central animal review committee established under the previous legislation.

Although it is not stipulated in the revised Act, it appears likely these would be local ethical review committees, specific to larger establishments. Smaller research establishments might need to use the committees set up at larger establishments. The structure of these committees is defined in the new Act which requires that they have at least seven members made up from equal numbers of experts in i) animal experiments, ii) alternative methods, iii) animal welfare, and iv) ethical assessment. At least two members must not be conducting animal experiments and at least three members, including the chairperson, must not be employed by a scientific institution applying to the committee.

The ethical review committees must be recognized by the Minister, who will be advised by the central animal review committee. This mechanism is to ensure they operate properly and, for the same purpose, all committees are required to submit an annual report to the Minister. An obligation of confidentiality is placed upon members of these committees with respect to information provided to them.

One addition to the legislation which has been discussed by many observers is the requirement to recognize the intrinsic value of animal life. However, the Act only states that "Any right accorded by or pursuant to this Act shall be exercised in recognition of the intrinsic value of animal life." It is noticeable that the ethical review committees are not required to take this point into account when assessing research plans.

Additional provisions introduced by the revised Act ban the LD50 and LC50 tests, but permit an exemption to be granted if it can be shown that the experiment cannot be performed by any other method. The testing of cosmetics and cosmetic ingredients is completely banned. Licensing for animal breeders and suppliers is required, applying similar provisions to those for animal use establishments.

The fact that the previous Act did not require the licensing of breeders and suppliers would mean that the Netherlands was not properly implementing the Directive 86/609 which requires such registration. It was obviously important for this to be corrected. The introduction of a system of research plan review based on the cost-benefit principle was also a positive move, bringing the Dutch system closer to that operating in the UK and Germany. However, with the introduction of a ban on the LD50 and an absolute ban on cosmetic testing, the Netherlands system has now gone significantly further than any other EU country. Naturally, much will depend on how the new Act is implemented but, on the basis of the written legislation, this appears to introduce a significantly tighter system of regulation in the Netherlands.



### **The Regulation of Animal Research and Testing in the United Kingdom**

The British system for regulating the use of animals in experiments is defined by a law passed in 1986 called the Animals (Scientific Procedures) Act. The main principle of this law is the requirement for researchers to obtain personal and project licences and a certificate for the establishment where the animal experimentation is conducted. [Ed. Note: A revision to the text of the Animals (Scientific Procedures) Act, which came into effect in September 1998, makes clear the requirement that a project licence applicant must be

aware of the possibilities of implementing any of the Three Rs (refinement, reduction and replacement of animal use) within the proposed study. One of the ways in which this awareness may be demonstrated is by documenting the literature searches which have been conducted in the course of planning the study.]

The legislation covers all vertebrate animals and has recently been extended to include the octopus. Anyone wanting to use any of these animals for a scientific purpose that might cause it distress, suffering or permanent harm must seek the necessary licences before commencing any animal work. There is a general exemption for animals which are humanely killed (using a method specified by the legislation) before being used in any experimentation or other procedure. Most of the normal laboratory species are required to be obtained from breeding or supplying establishments holding a certificate under this Act. Cats and dogs are required to be obtained directly from a certified breeder.

The personal licence lists the techniques the person is permitted to use on animals. Every time the researcher needs to use a new technique, the licence must be amended. The certificate for the establishment is given to a named person who is legally responsible for ensuring that the Act is properly enforced in the establishment. This person is normally the most senior person in charge or their deputy. They are required to have one named person (usually the chief animal technician) responsible for the care and welfare of the animals on a day-to-day basis. They are also required to have a named veterinary surgeon permanently on call.



A similar certificate is required by any premises breeding or supplying animals for scientific procedures. The standards of animal care and husbandry required in research, breeding and supplying establishments are defined in Codes of Practice published by the Home Office.

The project licence is held by the senior investigator in charge of a particular project or programme of testing. To apply for this licence they have to describe the scientific purpose behind the research project or testing scheme, the numbers and types of animals to be used, the procedures which the animals will go through and what steps have been taken to reduce the number of animals and any distress, suffering or harm involved. Project licences are valid for up to five years. All procedures within a project licence are assigned a severity limit - either mild, moderate or substantial. No animal procedure used under a project licence should exceed the severity limit unless an alteration to the licence has been agreed by the Inspector.

Applications for project licences are submitted to the Home Office which has a team of approximately 20 Inspectors (who must hold medical or veterinary qualifications and have relevant experience or training). These Inspectors will assess the application and may require it to be modified before granting the project licence. Home Office Inspectors pay unannounced visits to research establishments to ensure that researchers comply with their licences. They have the power to modify or suspend licences including, if necessary, the power to immediately suspend the certificate for an entire research establishment, halting all animal work.

Before a person is granted a personal licence, they are required to complete a specified training course normally lasting two or three days. A similar training requirement for all first-time applicants for project licences started in April 1995.

Project licence holders are required to keep detailed records of all animals used which are then reported annually to the Home Office. These annual statistics are published showing the numbers and types of animals used as well as the purposes for which they were used and the type of establishment using them.

A national committee (the Animal Procedures Committee), made up of researchers, veterinarians, doctors, lawyers, philosophers and animal welfarists advises the government about matters concerning the Act. This committee can decide which subjects it will study. It reviews all project licence applications in certain categories (cosmetic testing, tobacco research, etc) and has the power to see any other project licence application.

Although the UK system is complex and considered by some to be too bureaucratic, it is generally accepted by UK researchers as a fair and sensible system. There are some concerns that the Home Office requires too much detail in the project licence application. Since it is very difficult to predict the way that a fundamental research project will develop, researchers may need to submit several requests to vary the project licence to the Home Office which can delay the progress of the research.



## Laboratory Animal Research Legislation in Sweden

The Swedish system of regulating animal research comes under a general law controlling animal welfare, the Animal Protection Act and the Animal Protection Ordinance, both of 1988. To appreciate the way in which these regulate animal research, it is necessary to explain the way in which much of the legislation in Sweden operates.

Each Ministry in the Government has a number of National Boards operating under it. The legislation passed by the Parliament deals with the general principles and then delegates the power to create specific regulations to certain National Boards.

Under the Swedish Ministry for Agriculture, there is a National Board for Laboratory Animals which is responsible for setting up seven regional ethical committees. Scientific and medical experts make up half of the membership of each committee with the other half being lay members. Animal welfare representatives can only make up one third of the committee. The Chairman of each committee is a senior lawyer, usually a judge. Detailed rules for the operation of the committees are provided by the National Board for Laboratory Animals. All animal research and testing proposals are considered by these committees which are required to weigh up the importance of the experiments against the animal suffering involved. Projects can be approved for a maximum of three years. Although these committees only have advisory power, their recommendations are always followed. Animal experimentation conducted without ethical committee approval is illegal under the basic animal welfare provisions of the Animal Protection Act. There is no appeal against the decision of an ethical committee.

All animal research projects require ethical committee approval, including feeding studies, experiments under terminal anaesthesia and the killing of animals to remove tissues for use in vitro biomedical research.

It is worth noting that the Swedish legislation covers all animals, not just vertebrates. There is a general requirement that laboratory animals must be specially bred, but exceptions are granted for most types of animals apart from the normal laboratory species. Wild mammals are included in the exceptions. The re-use of animals is not banned under the Swedish system, but it is taken into account by the ethics committee when they assess the project proposal.

Veterinary inspectors from the local or regional authorities check research establishments to ensure compliance with the committee decisions. Where problems are found, they have the power to force researchers to comply with the committee recommendations or to impose a fine. However, the experimenter can appeal against this to the regional authorities of higher if necessary. In 1990, the law was amended to ensure that the ethical committee decision took precedence over the opinion of the inspector. The amendment ensured that when an animal research project was approved by an ethical committee and performed in accordance with the protocol approved by that committee, the inspector had no legal power to halt the project.

The Laboratory Animal Board is also responsible for the keeping of records and collection of statistical data about the numbers and type of animals used. They are also responsible for the

regulation of education and training requirements for experimenters and technicians and funding the development of alternatives methods to the use of laboratory animals.

In the National Board for Agriculture, there is a Department of Veterinary Affairs which has to approve the design of animal research facilities before they are built or before any significant modifications to the buildings are made. It licences the facility when it meets the guidelines for temperature control, humidity, cage sizes, etc. Each facility is required to appoint a supervisor, a person in charge of animal research for the facility who must be approved by the National Board of Agriculture. This Board also registers and approves laboratory animal breeders and suppliers.

All animal researchers, technicians and animal care[givers] are required to undergo training within two years of starting working with animals. Until they have completed this training and passed a test on it, they are required to work under supervision. The National Board for Laboratory Animals has set out a number of subjects which must be covered by the training, although no formal curriculum or duration of training is stipulated.

The National Board for Laboratory Animals also creates regulations about the recording of animal experiments and the reporting of statistical data. Regulations also cover the way that certain procedures must be conducted. These include immunizations, the production of monoclonal antibodies and acute toxicity testing.

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In Canada, promotion of the Three Rs concept of alternatives occurs largely through the Canadian Council on Animal Care. Institution-based animal care committees are required to conduct an ethical review of all protocols which use animals in research, teaching or testing. Investigators are expected to use animals only when their best efforts to find an alternative have failed. Those using animals are required to employ the most humane methods on the smallest number of animals possible. The Joseph F. Morgan Research Foundation was established to promote the development and use of alternative methods in Canada. The focus of the Foundation has been on the use of alternative methods for testing purposes. However,

the Foundation also encourages the acceptance of each of the Three Rs throughout Canadian science. The Foundation is therefore in the process of developing a refinement alternatives program.

Descriptors: animal experiments, animal welfare, animal testing alternatives..

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NAL call number: SF405.5 A3

Descriptors: ethical review process, regulations, functions of an AEEC, lay members, scientific review, advantages and disadvantages, consistency of review, Animal Procedures Committee, Home Office, Boyd Report.

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NAL call number: AHV4762 A3A64

Descriptors: Canadian Council on Animal Care, experimental animals, guidelines, ACUC.

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AB- The ethical evaluation of biomedical experiments is loyally accepted in the Netherlands. It was introduced everywhere during the last 15 years. Among the targets we find not only the protection of the experimental objects--animals and humans--but also the protection of researchers who may find moral support in the approval of their projects by a Committee of Ethical Evaluation. Concerning experiments in animals, the legal framework is provided by the Law on Animal Experiments. This law was drawn up in accordance with the directive of the E.U. To be allowed to practice experiments in animals, an institute must possess a licence; the researchers are moreover obliged to be appropriately trained with regard to experiments in animals. To that end an adequately functioning organization has been set up. The intensive supervision is widely decentralized and effected for the greater part by experts working within the institutes. The "intra muros" Committees supervising the experiments in animals play an important part in the ethical evaluation. More than 50 of those Committees are active at this time. Setting the ethical standards is done in close collaboration between the Authorities and the researchers. Researchers and animal protection associations have established a "Platform for the Replacement of Experiments in Animals", in which they support

development of alternative methods for research. The legislation concerning medical experiments in humans is not yet completely enforced, but in practice the ethical evaluation has been effected for many years in every hospital of the Netherlands. At present about 150 "Committees for medico-ethical evaluation" are at work. Their task may be very heavy, especially in the academic hospitals, where, mostly, over 150 projects are advised on every year. Adequate training facilities are provided for the members of the committees. The passing of the bill on experiments in humans is stagnating owing to political reasons. Besides the approval of the present practice, the bill-draft contains some elements that are difficult to accept by researchers; among other things, the researchers refuse a possible political influence on the ethical advice. Moreover, there exists a menace to see the insurers changing their rules: the legislation on privacy might also hamper the development of a research seeming too closely patient-linked. Sufficient attention is not given to the financial aspects of the evaluation-process. The real cost of the evaluation should be incorporated into the budget of research projects.

Descriptors: animal testing alternatives, legislation and jurisprudence, ethics committees, human experimentation, Netherlands.

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Descriptors: animal welfare, laboratory animals, regulations, law enforcement.

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Descriptors: animal welfare, education, animal ethics committee, scientific animal use, Australian Code of Practice.

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Descriptors: animal welfare, animal experiments, ethics..



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 Descriptors: animal welfare, pain, prevention, legislation, protection, animal testing alternatives.
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 NAL call number: QL737 P9J66  
 Descriptors: laboratory animals, ethics, research, ACUC.
- Scharmann, W. (1994). **Housing of laboratory animals and animal welfare legislation: a critical evaluation of current guidelines. [Tiergerechte Haltung von Versuchstieren: Kritische Bewertung der geltenden Richtlinien.]** *Tierärztliche Umschau* 49(9): 552, 555-560.  
 NAL call number: 41.8 T445  
 Descriptors: rats, mice, rabbits, guinea pigs, caging, housing, European Union, experiments, animal welfare, guidelines, legislation and regulations.
- Swiss Academy of Medical Sciences and Swiss Academy of Sciences (1992). **Ethical principles and guidelines for scientific experiments on animals.** *Experientia* 48(1):1-3.  
 NAL call number: 475 EX7.  
 Descriptors: animal welfare, animal experiments, guidelines, professional ethics.
- Townsend, P. and D.B. Morton (1995). **Laboratory animal care policies and regulations: United Kingdom.** *ILAR Journal* 37 (2): 68-74.  
 NAL call number: QL55.A1I43.  
 Descriptors: animal welfare, regulations, law enforcement, laboratory animals..
- Wong, J. (1995). **Laboratory animal care policies and regulations: Canada.** *ILAR Journal* 37 (2): 57-59.  
 NAL call number: QL55.A1I43.  
 Descriptors: animal welfare, laboratory animals, regulations, law enforcement, organizations.



## Useful World Wide Web Sites

### **Animals (Scientific Procedures) Act - 1986**

<http://www.homeoffice.gov.uk/animact/aspag1.htm>

From the United Kingdom Home Office-full text, plus amendments and guidance notes

### **The Animal Welfare Act and the Animal Welfare Ordinance (Sweden)**

<http://www.algonet.se/~stifud/act-ordinance.html>

Made available by the Swedish Fund for Research Without Animal Experiments

### **The Dutch Experiments on Animals Act**

<http://www.pdk.dgk.ruu.nl/nca/act/wetopdp.htm>

Provided by the Netherlands Center for Alternatives-in English.

### **European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes**

<http://www.coe.fr/eng/legaltxt/123e.htm>

The Convention is designed primarily to reduce both the number of experiments and the number of animals used for such purposes. It encourages Parties not to experiment on animals except where there is no alternative. All research into alternative methods should be encouraged. Animals to be experimented on should be selected on the basis of clearly established quantitative criteria and must be well cared for and spared avoidable suffering whenever possible. To this end, the Convention lays down a number of principles which are to be considered only as a starting point. The Parties meet regularly to examine the application of the Convention and, if appropriate, to extend or strengthen its provisions.

### **Laboratory Animals—Articles to Download**

<http://www.lal.org.uk/pdf.htm>

This site provides access to many Working Party Reports, FELASA reports, and scientific papers from European scientists.

### **Legislation Worldwide**

<http://www.frame-uk.demon.co.uk/Links/worldlaws.htm>

From FRAME in the United Kingdom

### **The National Board for Laboratory Animals (Centrala försöksdjursnämnden, CFN)**

<http://www.algonet.se/~stifud/nbla.html>

An overview of this Swedish Government agency - from the Swedish Fund for Research Without Animal Experiments.

### **Norwegian Regulation of Animal Experimentation (Forskrift om forsøk med dyr)**

<http://oslovet.veths.no/statute.html>

Pronounced by the Ministry of Agriculture, January 15, 1996, in accordance with the Animal Welfare Act of December 12, 1974, nr 73, §§22 and 30, after royal proclamation of 19.11.76, amended November 17, 1998.

**University of Melbourne**

<http://www.unimelb.edu.au/research/ethics/aee/index.htm>

The homepage of the Animal Experimentation Ethics Committee containing guidelines, policies and recommendations.

**University of Northern British Columbia**

<http://quarles.unbc.edu/research/animal.html>

Policy and Procedures on Animal Care from the Office of Research and Graduate Studies.



# Primary References







In the primary reference material for the Institutional Animal Care and Use Committee, the annotated citations are mostly books and conference proceedings, with the exception of legislation, and cover 1985 to December 1998.

While there has been an attempt to cross-reference citations that can appropriately fit into more than one category, please examine related categories for the desired information. For example, a book on rodent surgery may be found in “Rodents and Rabbits” and/or “Surgery”. It may also be found in “General Laboratory Animal Care and Use” if a book contains information about several species including a chapter on rodent medicine.

## Contents

- Agricultural Animals
- Alternatives
- Anesthesia, Analgesia, and Euthanasia
- Animal Care and Use Committees
- Cats and Dogs
- Disease and Parasites
- Ectotherms (Amphibians, Fish, Reptiles)
- Formularies
- General Laboratory Animal Care and Use
- Genetics and Transgenics
- Invertebrates
- Laboratory Animal Housing
- Legislation, Policies, and Guidelines
- Medical and Veterinary Dictionaries
- Occupational Safety
- Philosophy and Ethics
- Primates (Nonhuman)
- Rabbits and Rodents
- Surgery
- Wild Animals

## Agricultural Animals

- Alton, G.G. (1990). *Veterinary Diagnostic Bacteriology: A Manual of Laboratory Procedures for Selected Diseases of Livestock*. Food and Agriculture Organization of the United Nations: Rome, 81p.  
NAL call number: SF1.F64 no.81  
A manual of bacteriology methods for use with agricultural animal epidemiology.
- Barrick, R.K. and H.L. Harmon (1988). *Animal Production and Management*. McGraw-Hill Book Company: New York, NY, 402p.  
NAL call number: SF61.B35.  
This book was developed as a textbook to emphasize the management of animals on farms and ranches, not just the production of animals and animal products. It highlights basic production and dwells on management skills and techniques.
- Blakely, J. and D. Bade (1994). *The Science of Animal Husbandry*, 6th edition. Prentice Hall Career and Technology: Englewood Cliffs, NJ, 656p.  
NAL call number: SF61.B56.  
This is an introductory textbook for the college student. Provides a condensed, highly illustrated, easy-to-read version of animal science, while keeping in mind the needs of the instructor.
- Consortium for Developing a Guide for the Care and Use of Agricultural Animals in Research and Teaching (1998). *Guide for the Care and Use of Agricultural Animals in Agricultural Research and Teaching*. Federation of Animal Science Societies, 1111 North Dunlap Ave., Savoy, IL 61874, 89p.  
NAL call number: QL55.G8.  
Primary reference developed by and for those using agricultural animals in research and teaching. It is meant to serve as an independent reference for the care and use of agricultural animals. It provides information on the most common agricultural animals under a variety of teaching and research conditions. Referred to for biomedical research involving agricultural animals by the National Institutes of Health, Office of Protection from Research Risks and the Association for the Assessment and Accreditation of Laboratory Animal Care International.
- Hannon, J.P. and C.E. Wade (1989). *Normal Physiological Values for Conscious Pigs Used in Biomedical Research*. LAIR, Military Trauma Research: San Francisco, CA, 19p.  
NAL call number: SF768.2.S95H3  
Reference values for over 100 physiologic or related variables. Included are body composition, fluid volumes, blood gas, hormone levels, hemodynamics, renal function, and more.
- Herman, H.A.; J.R. Mitchell; and G.A. Doak (1994). *The Artificial Insemination and Embryo Transfer of Dairy and Beef Cattle (including information pertaining to goats, sheep, horses, swine, and other animals) : A Handbook and Laboratory Manual for Students, Herd Operators, and Persons Involved in Genetic Improvement*, 8th edition. Interstate Printers & Publishers: Danville, IL, 382p.

NAL call number: SF201.5.H45 1994

Methods for artificial insemination and embryo transfer in cattle. Much of the information is applicable to other agricultural species.

Mench, J.A., S.J. Mayer, and L. Krulisch (1992). *The Well-being of Agricultural Animals in Biomedical and Agricultural Research*. Scientists Center for Animal Welfare: Greenbelt, MD, 112p.

NAL call number: HV4704.W38 1990

Conference proceedings which include papers about regulatory perspectives, animal care and management, a summaries of workshops on specific species. Topics include handling and transport, stress, restraint, housing, and husbandry.

Mench, J.A. and W.R. Stricklin, eds. (1993). **An International Conference on Farm Animal Welfare: Ethical, Technological, and Sociopolitical Perspectives.** *Journal of Agricultural and Environmental Ethics* 6(Suppl. 1):1-154. **An International Conference on Farm Animal Welfare: Scientific Perspectives.** *Journal of Agricultural and Environmental Ethics* 6(Suppl. 2):1-116.

NAL call number: BJ52.5 J68

A two-volume set of conference proceedings that discuss agricultural animal welfare from ethical, technological, sociopolitical, and scientific perspectives. A balanced and informative introduction to the concept and applicability of animal welfare as it pertains to farm animals.

Swindle, M.M.; D.C. Moody; and L.D. Phillips, eds. (1992). *Swine as Models in Biomedical Research*. Iowa State University Press: Ames, IA, 312p.

NAL call number: RB125 S79 1992

Proceedings of the Seventh Charles River International Symposium which was held in 1989. Reviews all aspects of swine care and use in biomedical research.

Taylor, R.E. (1995). *Scientific Farm Animal Production: An Introduction to Animal Science*, 5th edition. Prentice Hall: Englewood Cliffs, NJ, 672p.

NAL call number: SF61.B63.

An overview of the biological principles applicable to animal science with chapters on reproduction, genetics, nutrition, lactation, end breeding, and management of agricultural animal species. It is designed for the introductory animal science courses.

Tumbleson, M.E., ed. (1986). *Swine in Biomedical Research*. Plenum Press: New York, NY. 1986.

NAL call number: RB125.C68.

This book the proceedings of a 1985 conference on swine in biomedical research and is a three-volume set. Contains comprehensive coverage of swine as models for a variety of biomedical studies, such as alcoholism, diabetes, digestive disorders, organ transplantation, atherosclerosis, gingivitis, hypertension, exercise, hypotension, cancer, osteochondrosis, dermal healing and septic shock. This book was designed as a reference to be used as a data base for future investigations.

Universities Federation for Animal Welfare (1988). *Management and Welfare of Farm Animals*. Bailliere Tindall: London, England, 260p.

NAL call number: SF61.M35



Describes strategies designed to improve the efficiency, standards, housing, and care of farm animals and production. Emphasis is given to the welfare implications of modern husbandry techniques and promotes a humane attitude for those responsible for the care, management and welfare of farm animals.

## Alternatives

*Alternatives to Laboratory Animals*. Available from: Fund for the Replacement of Animals in Medical Experiments (FRAME), Eastgate House, 34 Stoney Street, Nottingham, NG1 1NB, England.

NAL call number: Z7994.L3A5.

Quarterly journal covering all aspects of the development, introduction, and use of alternatives in animal research and testing. Includes some highly technical articles but many are comprehensible to the non-scientist. "Book Reviews" and "Selected Titles" sections provide current references for further reading on specific topics.

*ALTEX: Alternativen Zu Tierexperimenten*. Available from: ALTEX, Postfach 100125, D-78401 Konstanz, Email: [altex@bluewin.ch](mailto:altex@bluewin.ch), <http://www.zet.bartl.net/ALTEX/index.htm>

NAL call number: HV4915 A47 1996

Peer reviewed official journal of the Mitteleuropäischen Gesellschaft für Alternativmethoden zu Tierversuchen (MGAT). Articles are in German with English and German abstracts. Many articles describe new methods of replacement although reduction and refinement are also included.

Australian and New Zealand Council for the Care of Animals in Research and Teaching (ANZCCART) (1993). *Alternatives to the Use of Animals in Undergraduate Teaching in Australia and New Zealand*. ANZCCART: Glen Osmond, SA [Australia], 27 p.

NAL call number: QL55.A48 1993

A list of bibliographic citations for alternatives to the use of animals in teaching undergraduates.

Balls, M.; J. Bridges, J. Southee (1991). *Animals and Alternatives in Toxicology: Present Status and Future Prospects*. VCH Publishers: New York, N.Y., 390p.

NAL call number: RA1199.4.A54A53 1991

Based on the proceedings of a meeting held on Nov. 12-13, 1990 to discuss the report of the FRAME Toxicity Committee.

Hudson, V. (1997). *Alternatives to the Use of Live Vertebrates in Biomedical Research and Testing: A Bibliography with Abstracts*. No. 2. National Library of Medicine: Bethesda, MD, 145p.

NAL call number: Z7994 L3A483

Literature citations and abstracts from the National Library of Medicine databases. Citations address Reduction, Refinement, and Replacement. They are grouped by study areas including carcinogenesis, cytotoxicity, dermal toxicity, pharmacokinetic and mechanistic studies, and others. Available in hardcopy and electronically from <http://sis.nlm.nih.gov>

*The Johns Hopkins Center for Alternatives to Animal Testing*. Available from: Center for Alternatives to Animal Testing, Johns Hopkins School of Public Health, 111 Market Place,

Suite 840, Baltimore, MD 21202-6709, tel: (410) 223-1693, fax: (410) 223-1603, email: CAAT@CAAT.spharbor.jhu.edu  
NAL call number: HV4701.J6.

A quarterly newsletter that reports new developments in alternative approaches to whole animal studies for evaluating the safety of chemical products, funding opportunities, and meetings.

Johns Hopkins University, School of Hygiene and Public Health (1992). *Animal Care and Use Committees and Alternatives: A Symposium Sponsored by the Johns Hopkins School of Hygiene and Public Health, Office for Research Subjects, June 18, 1992*. Johns Hopkins Center for Alternatives to Animal Testing: Baltimore, MD, 110p.  
NAL call number: HV4704.A53 1992  
Proceedings from the symposium.

Kapis, M.B. and S.C. Gad, eds. (1993). *Non-Animal Techniques in Biomedical and Behavioral Research and Testing*. CRC Press: Boca Raton, FL, 264p.  
NAL call number: R852.N65 1993  
Contains chapters on alternatives to whole animal testing, specific in vitro examples in cosmetic and pharmaceutical industries, use of computational models, network models, magnetic resonance, physicochemical techniques, and alternatives in neurosciences, psychiatry, ethology, molecular biology, and genetics.

Kimm, V.J. (1988). *Alternative Methodology for Acute Toxicity Testing*. U.S. Environmental Protection Agency, Office of Pesticides and Toxic Substances: Washington, DC, 10p.  
NAL call number: HV4928.U5  
Revised policy for acute toxicity testing.

Larson, J.A. (1995). *Directory of Resources on Alternatives and Animal Use in the Life Sciences*, 1st ed. AWIC Resource Series, 1082-9644 ; no. 1. U.S. Dept. of Agriculture, National Agricultural Library, Animal Welfare Information Center, Beltsville, MD, 65p.  
NAL call number: aHV4701.A94 no.1  
A directory of audiovisuals, journals, newsletters, and other resources for information about alternatives in animal research, teaching, and testing.

Lembeck, F., ed. (1989). *Scientific Alternatives to Animal Experiments*. Ellis Horwood Limited: Chichester, West Sussex, PO19 1EB, England.  
NAL call number: QL51.A48  
Alternatives in the use of animals for teaching, testing, and research are discussed in 37 chapters. Topics include research in neurochemistry, genetics, immunology, behavior, drug development, and cancer research. Determining appropriate animal numbers, unnecessary duplication of studies, and methodology are also examined.

Mehlman, M.A., ed. (1989). *Benchmarks: Alternative Methods in Toxicology*. Princeton Scientific Publishing Co., Inc.: Princeton, NJ, 219p.  
NAL call number: RA1231.T7B45.  
This volume, the first in a series, is intended to aid in the rapid identification, validation, and implementation of alternative methods in toxicology.

- National Association of Biology Teachers (1990). *The Responsible Use of Animals in Biology Classrooms: Including Alternatives to Dissection*. National Association of Biology Teachers: Reston, VA, 146p.  
NAL call number: QL55.R48  
Discusses the care and use of animals and suggests alternative teaching strategies.
- Office of Technology Assessment (1988). *Alternatives to Animal Use in Research, Testing, and Education*. Congress of the United States. M. Dekker: New York.  
NAL call number: QL51.2.U6A48.  
Analysis of the scientific, legal, economic, and ethical issues regarding alternatives to animal use for toxicity testing, biomedical and behavioral research, and education. Advisory panelists represent groups with widely varying interests and opinions such as animal welfare organizations, academic institutions, private industry, government agencies, and the concerned public. A fifty page summary of this book is also available from the Office of Technology Assessment in Washington, DC.
- Payne, J.W., ed. (1989). *In Vitro Techniques in Research: Recent Advances*. Open University Press: Philadelphia, PA.  
NAL call number: R853.T58I5.  
Papers in this book formed the greatest part of The Humane Research Trust Conference entitled *Recent advances in the Use of in vitro Techniques*. Discussed are several in vitro techniques using human tissues and cell culture.
- Physicians Committee for Responsible Medicine (PCRM) (1988). *Alternatives in Medical Education: Non-animal Methods*. PCRM: Washington, D.C., 16p.  
NAL call number: R835.A4  
Describes and gives contact information about computer simulations, models, and audiovisuals useful in replacing live animals in some areas of medical education.
- Reinhardt, C.A. (1994). *Alternatives to Animal Testing: New Ways in the Biomedical Sciences, Trends, and Progress*. VCH: New York, NY, 182p.  
NAL call number: RA1199.4.I5A44 1994  
Contains the main presentations made at the symposium Alternatives to Animal Testing, held at the ETH Zurich, Nov. 30, 1992, reviewed and updated to include developments up to fall 1993. Gives international perspectives, discusses particular methods, validation of alternatives, and legislation.
- Russell, W.M.S. and R.L. Burch (1992). *The Principles of Humane Experimental Technique*. Universities Federation for Animal Welfare: Wheathampstead, Herts, U.K., 238p.  
NAL call number: QL55.R8  
This is a reprint of the classic 1959 book that introduced the concepts of replacement, reduction, and refinement as they relate to the use of animals for research, testing, and education.
- Salem, H. (1995). *Animal Test Alternatives: Refinement, Reduction, Replacement*. M. Dekker: New York, NY, 349p.  
NAL call number: RA1199.A533 1995  
Examines alternatives in light of the regulatory climate and evaluates new technologies.



Schuppan, D. and W. Hardegg (1988). *Animal Protection by Alternatives*. [Tierschutz durch Alternativen : Symposium der Medizinischen Gesamtfakultat der Ruprecht-Karls-Universität Heidelberg und des Bundesverbandes der Pharmazeutischen Industrie e.V., 7.-9. September 1986, Heidelberg]. G. Fischer: Stuttgart, Germany and New York, NY, 150p.

NAL call number: HV4913.T53

Papers from a conference held in Heidelberg in 1986. All papers except one are in German.

Universities Federation for Animal Welfare and British Universities Film & Video Council (1988). *Animals in Science Teaching: A Directory of Audio Visual Alternatives*. British Universities Film & Video Council ; Universities Federation for Animal Welfare: Wheathampstead, Herts, U.K. 60p.

NAL call number: QL57.A49

A list of 290 audiovisuals for use as alternatives to the use of animals in education and research.

Van Zutphen, L.F.M. and M. Balls (1997). *Animal Alternatives, Welfare and Ethics*. Elsevier: Amsterdam, New York, Oxford, Tokyo, 1260p.

NAL call number: QL1 D48 v.27

The proceedings of the 2nd World Congress on Alternatives and Animal Use in the Life Sciences held in 1996. Includes plenary lectures and papers on national and regional developments, animal welfare and refinement, transgenic animals, scientific procedures and humane endpoints, noninvasive methods, ethics, databases, education, toxicity testing, pharmacology, testing medical devices, antibody and blood products, antibody production techniques, and validation and acceptance of alternatives.

Webber, M., ed. (1988). *In Vitro Models for Cancer Research: Carcinoma of the Prostate and Testis*. CRC Press, Inc.: Boca Raton, FL.

NAL call number: RC267.I48 v.5.

This volume describes cell and organ culture systems that provide for the study of normal and neoplastic prostate and testes. The role of trace elements and hormones on the prostate are explored through in vitro techniques. Authors suggest ways in which in vitro testing can be used to study carcinogenesis, tumor prevention, and treatment.

Zinko, U.; N. Jukes, and C. Gericke (1997). *From Guinea Pig to Computer Mouse*. EuroNICHE, 11 Beckingham Rd., Leicester LE2 1HB, UK; tel/fax +44(0)181 341 9115; email: lynx@gn.apc.org ; 229p.

EuroNICHE (European Network of Individuals and Campaigns for Humane Education) provides this annotated catalog of audiovisuals, computer simulations, videodisks, and models for teaching anatomy, physiology, anesthesia, behavior, surgery, and other subjects taught in high school through graduate levels. Contact information and prices are given.

Zurlo, J., D. Rudacille, and A.M. Goldberg (1994). *Animals and Alternatives in Testing: History, Science, and Ethics*. Mary Ann Liebert, Inc.: New York, NY, 86p.

Covers ethical, legal, and historical issues in the development of alternative methods.

Emphasis is on toxicity testing, vaccine development, in vitro methods, and validation.

Contains timelines of animal welfare in the U.S. and U.K., tissue culture, in vitro toxicology, and methods of vaccine development.



## Anesthesia, Analgesia, and Euthanasia

Andrews, E.J., B.T. Bennett, J.D. Clark, K.A. Houpt, P.J. Pascoe, G.W. Robinson, and J.R. Boyce (1993). **1993 Report of the AVMA panel on euthanasia.** *Journal of the American Veterinary Medical Association* 202(2):229-249.

NAL call number: 41.8 Am3

A comprehensive list of chemical and physical methods of euthanasia, modes of action, special considerations, and the advantages and disadvantages of each.

Close, B., K. Banister, V. Baumans, E. Bernoth, N. Bromage, J. Bunyan, W. Erhardt, P. Flecknell, N. Gregory, H. Hackbarth, D. Morton, and C. Warwick (1997, 1996). **Recommendations for euthanasia of experimental animals: report of a working party.** *Laboratory Animals* 31:1-32, 30:293-316.

NAL call number: QL55.A1L3

This document was prepared in response to European Commission Directive 86/609/EEC.

The first two sections are in the 1996 issue and cover euthanasia objectives, signs of pain and distress, recognition of death, personnel training, equipment, carcass disposal, and acceptable and unacceptable methods of euthanasia. It also includes an extensive bibliography covering general euthanasia, fish, amphibians, reptiles, birds, rodents, rabbits, carnivores, large mammals, primates, and exotics. The third section, published in 1997, describes methods of euthanasia for each species group and euthanasia training materials.

Flecknell, P.A. (1996). *Laboratory Animal Anaesthesia: A Practical Introduction for Research Workers and Technicians.* 2nd edition. Academic Press: San Diego, CA, NY, 274p.

NAL call number: SF77.F54 1996

Provides basic information about anesthesia to research technicians who have not received extensive training in this field. Sections emphasize the principles of pre- and post-operative care, anesthetic techniques and equipment, and pain recognition and alleviation.

Grier, R.L., T.L. Colvin, and L.N. Kopecky (1990). *Euthanasia Guide for Animal Shelters.* 3rd edition. Moss Creek Publications: Ames, IA, 47p.

NAL call number: SF914.G74 1990

Handbook for euthanasia of companion animals in animal shelters.

Institute of Laboratory Animal Resources Committee on Pain and Distress in Laboratory Animals (1992). *Recognition and Alleviation of Pain and Distress in Laboratory Animals.*

National Academy Press: Washington, DC, 137p.

NAL call number: SF996.5.R43 1992

Covers the biology of pain, stress and distress, recognition, control, euthanasia, and recommendations for specific animals.

Kohn, D.F., et al., eds. (1997). *Anesthesia and Analgesia in Laboratory Animals.* Academic Press: San Diego, CA, 426p.

NAL call number: SF996.5 A54 1997

Covers pharmacology, monitoring, paralytic agents, post surgical care, equipment, and many other topics.

- Kreger, M.D. (1997). *Animal Euthanasia*. Special Reference Brief 98-01. National Agricultural Library: Beltsville, MD, 48p.  
NAL call number: aS21 D27S64  
Multidatabase literature search resulting in 223 animal euthanasia citations. Some citations include abstracts. Citations cover methods used for companion, livestock, zoo, and laboratory animals. Many citations deal with grief over pet loss and the veterinarian/client relationship.
- Ross, L.G. and B. Ross (1984). *Anaesthetic and Sedative Techniques for Fish*. Institute of Aquaculture, University of Scotland: Sterling, Scotland, 35p.  
NAL call number: SH156.9.R6  
A guide to anaesthetic and sedative techniques for fish used in laboratory and field research.
- UFAW (1989). *Guidelines on the Care of Laboratory Animals and Their Use for Scientific Purposes: II - Pain, Analgesia and Anaesthesia*. Universities Federation for Animal Welfare: Wheathampstead, Herts, U.K., 30p.  
NAL call number: SF406.G8 v.2.  
This document provides recommendations for recognizing laboratory animal pain symptoms, minimization and control by use of analgesic and anesthetic agents, and post-anesthetic care.
- UFAW (1986). *Euthanasia of Unwanted, Injured or Diseased Animals or for Educational of Scientific Purposes*. Universities Federation for Animal Welfare: Wheathampstead, Herts, U.K., 51p.  
NAL call number: HV4731 E9 1986  
Symposium proceedings with papers by many authors. Includes covers companion animals, reptiles and amphibians, and other species.

## Animal Care and Use Committees

- Animal Welfare Information Center (AWIC). *Animal Welfare Information Center Newsletter*. National Agricultural Library, AWIC, 10301 Baltimore Ave., Beltsville, MD 20705.  
NAL call number: AHV4701.A952  
This newsletter covers a wide range of topics relevant to the scientific community and the IACUC. Topics include animal welfare regulations, Animal Care and Use Committees, agricultural animal care, alternatives, legislation updates, upcoming meeting, funding sources, new AWIC products and services, and scientific and general articles on animal care and use issues and methods. Subscriptions are free. Back issues are available on the AWIC website: <http://www.nal.usda.gov/awic>
- Berry, D. (1991). *Reference Materials for Members of Animal Care and Use Committees*. National Agricultural Library, Animal Welfare Information Center: Beltsville, MD, 42p.  
NAL call number: aHV4701.A95 no.10  
Annotated bibliography of books and proceedings about animal care and use committees covering 1977 to 1991.

- Canadian Council on Animal Care (1992). *Animal Care Committees: Role and Responsibilities*. Canadian Council on Animal Care: Ottawa, Ontario, Canada, 145p.  
NAL call number: HV4708 A55 1992  
Proceedings from a workshop sponsored by the Canadian Council on Animal Care (CCAC) in February 1992. Topics include researcher responsibilities, ethical concerns, psychology protocol reviews, media concerns, CCAC Alternatives Committee, peer review, occupational health and safety, training personnel, monitoring field studies, invertebrates, and workshop reports.
- Canadian Federation of Humane Societies (1986). *Guidelines for Lay Members of Animal Care Committees*. Revised 1986. Canadian Federation of Humane Societies: Nepean, Ontario.  
NAL call number: HV4735.G8.  
Describes the functions and activities of animal care committees. Includes sections entitled "Lay committee members: special people with special problems", "How to review protocols", and "Pain".
- Council of the Applied Research Ethics National Association (ARENA) (1992). *Institutional Animal Care and Use Committee Guidebook*. National Institutes of Health Publication No. 92-3415, National Institutes of Health: Bethesda, MD, 60p.  
NAL call number: HV4764.I58 1992  
Excellent overview of Institutional Animal Care and Use Committee composition, function, proposal review, oversight of the animal care and use program, record keeping, sample forms, and special considerations. Useful review of NIH policies and the Animal Welfare Act as they pertain to the committee.
- Editorial Committee of Institutional Administrators and Laboratory Animal Specialists for the Henry M. Jackson Foundation for Advancement of Military Medicine, Uniformed Services University of Health Sciences (1988). *Institutional Administrator's Manual for Laboratory Animal Care and Use*. Bethesda, MD: U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, 82p. Available from: Office for Protection from Research Risks, National Institutes of Health, 6100 Executive Blvd., Suite B01, Rockville, MD 20892-7507.  
NAL call number: SF406 I54  
A guide for institutional administrators who supervise laboratory animal care and use programs. The manual addresses questions involving quality care, ethics, and legal requirements for animal care and use programs.
- Guttman, H.N.; J.A. Mench; and R.C. Simmonds, eds. (1989). *Science and Animals: Addressing Contemporary Issues*. Scientists Center for Animal Welfare: Greenbelt, MD, 149p.  
NAL call number: HV4704.S33.  
Proceedings from a conference held by the Scientists Center for Animal Welfare in 1988. "Community and Lay Members of Animal Care and Use Committees", "Animal Care and Use Committee Issues", and "Well-Being and Ethics" are three of the six sections contained in this volume. The community and lay member session was developed and presented entirely by active community and lay members of Animal Care and Use Committees.
- Johns Hopkins University, School of Hygiene and Public Health (1992). *Animal Care and Use Committees and Alternatives: A Symposium Sponsored by the Johns Hopkins School of*



*Hygiene and Public Health, Office for Research Subjects, June 18, 1992.* Johns Hopkins Center for Alternatives to Animal Testing: Baltimore, MD, 110p.

NAL call number: HV4704.A53 1992

Transcript of lectures about the concept of alternatives, their use in science, information resources, regulatory requirements, and ACUC involvement in pre-college education.

*Lab Animal* (May 1997). 26:5.

NAL call number: QL55.A1L33

Special issue devoted to IACUCs. Includes *Do pressure and prejudice influence the IACUC?* by J. Silverman, *The SCAW IACUC survey part I: preliminary results* by L. Krulisch and J. Mench, *The SCAW IACUC survey part II: the unaffiliated member* by P. Theran, and *Resource: IACUCs and the World Wide Web* by K. Boschert.

Laboratory Animal Science Association and Universities Federation for Animal Welfare (1990). *Guidelines on the Care of Laboratory Animals and Their Use for Scientific Purposes: IV - Planning and Design of Experiments.* Ennisfield Ltd.: London, England, 20p.

NAL call number: SF406.G8 v.4.

Basic recommendations as to the planning, and design of experiments using animals, and how this can effect the outcome of the experiment.

National Institutes of Health and Office of Protection from Research Risks and NIH Office of Animal Care and Use (1989). *Animal Care and Use: Policy Issues in the 1990s.* Office of Animal Care and Use, National Institutes of Health: Bethesda, MD, 79p.

NAL call number: HV4704.A46 1989

Proceedings from NIH OPRR/OACU conference, November 16-17, 1989, Bethesda, Maryland.

National Institutes of Health Animal Research Committee (1994). *Using Animals in Intramural Research: Guidelines for Investigators and Guidelines for Animal Users.* NIH Office of Animal Care and Use: Bethesda, MD.

NAL call number: HV4928.U85 1994

NIH Research Advisory Committee notebook outlining the NIH ACUC program, occupational safety, laws and regulations, ethical and scientific issues, alternatives, pain and distress, and other topics.

Orlans, F.B. (1987). **Research Protocol Review for Animal Welfare.** *Investigative Radiology* 22:253-258.

An overview of protocol review, investigators' concerns about ACUC's, and assessing and minimizing animal pain and distress.

Orlans, F.B. (1988). **Field Research Guidelines: Impact on Animal Care and Use Committees.** Scientists Center for Animal Welfare: Greenbelt, MD, 23p.

NAL call number: HV4704.F5

The proceedings of a workshop entitled "Field Research Standards" held October 8, 1987.

Orlans, F.B.; R.C. Simmonds; and W.J. Dodds, eds. (1987). **Effective Animal Care and Use Committees.** *Laboratory Animal Science*, Special Issue (January 1987), 178p. Scientists



Center for Animal Welfare, Golden Triangle Building One, 7833 Walker Dr., Suite 340, Greenbelt, MD 20770, email: scaw@erols.com.

NAL call number: 410.9 P94.

Papers from workshops sponsored by the Scientists Center for Animal Welfare focusing on effective review of biomedical experiments to ensure humane and appropriate use of animals. Includes chapters concerning the objectives and activities of animal care and use committees, protocol review and animal pain, and roles of committee members (including lay members).

Public Responsibility in Medicine and Research (PRIM&R) and Tufts University School of Medicine (1991). *Animal Care and Use Programs: Regulatory Compliance and Education in an Age of Fiscal Constraint*. PRIM&R: Boston, MA, 408p.

NAL call number: HV4913.A54

Educational material for: Animal care and use programs.

Scientists Center for Animal Welfare (SCAW). *SCAW Newsletter*. Golden Triangle Building One, 7833 Walker Dr., Suite 340, Greenbelt, MD 20770, tel: (301) 345-3500, fax: (301) 345-3503, email: scaw@erols.com

NAL call number: QL55.N48.

Quarterly newsletter that promotes the humane treatment of animals used in research. Articles frequently focus on animal care and use committees.

United States Department of Agriculture (1990). *Directive 635.1, Humane Care and Use*. .

U.S. Dept. of Agriculture, Agricultural Research Service: Washington, D.C.

NAL call number: aKF3841.D57--1990

Description of requirements for animal care and animal care and use protocols for use by USDA, Agricultural Research Service researchers and veterinary staff.

United States Department of Defense (1995). *Report to the Senate Armed Services Committee and the House of Representatives National Security Committee on Department of Defense Animal Care and Use Programs*. Department of Defense: Washington, D.C.

NAL call number: HV4928.U56 1995

The Fiscal Year 1995 report to Congress on the Department of Defense animal care and use programs in research, education, and training for Defense and extramural projects.

University of Texas Health Science Center at San Antonio (1990). *Responsible Care and Use of Animals in Research and Training: Institutional Animal Care Training Program*. University of Texas Health Science Center at San Antonio: San Antonio, TX, 36p.

NAL call number: HV4933.T4U5

Description of the university's program, relevant legislation, alternatives, organization resources, zoonoses, facilities, and animal health management.

## Cats and Dogs

Askew, H.R. (1996). *Treatment of Behavior Problems in Dogs and Cats: A Guide for the Small Animal Veterinarian*. Blackwell Science: Oxford; Cambridge, MA, 350p.

NAL call number: SF433.A85 1996

Covers pet behavior counseling and treatment of dog and cat behavioral problems such as aggression, fear, separation anxiety, and elimination.

August, J.R. (1997). *Consultations in Feline Internal Medicine* 3. W.B. Saunders: Philadelphia, PA, 673p.

NAL call number: SF985.C65 1997

Reviews infectious diseases, disease and treatment of each biological systems, oncology, dermatology, and population medicine.

Bordwell, S. (1994). *The American Animal Hospital Association Encyclopedia of Dog Health and Care*. Hearst Books: New York, 292p.

NAL call number: SF427.B625 1994

Basic care, behavior, vaccinations, and disease recognition and treatment. Also covers conditions specific to puppies, males, females, first aid, emergency procedures, and poison control.

Chandler, E.A. (1991). *Canine Medicine and Therapeutics*. 3rd edition. Blackwell Scientific Publications: St Louis, MO, 876p.

NAL call number: SF767.D6C3 1991

Reviews organ systems, nutrition, behavior, parasites, clinical biochemistry, and clinical pharmacology.

Chandler, E.A., C.J. Gaskell, and M. Rosalind, eds. (1994). *Feline Medicine and Therapeutics*. 2nd edition. Blackwell Scientific: Oxford; Boston, MA, 705p.

NAL call number: SF985.F45 1994

Covers the major organ systems, specific viruses, diagnosis and treatment, pharmacology, poisoning, therapeutics, and behavioral problems.

Crow, S.E. and S.O. Walshaw (1997). *Manual of Clinical Procedures in the Dog, Cat, and Rabbit*. 2nd edition. Lippincott-Raven: New York, NY, 323p.

NAL call number: SF991 C76 1997

The purpose of this manual is to provide information on the correct use of diagnostic and therapeutic procedures in veterinary practice. It is a useful tool for veterinary technologists, veterinary students, as well as veterinarians and veterinary technicians in small animal practice or laboratory animal care facilities. The text is organized by procedures, with each described in a step-by-step manner.

Donnersberger, A.B.; A.E. Lesak, and M.J. Timmons (1989). *A Laboratory Textbook of Anatomy and Physiology: The Cat*. 4th edition. D.C. Heath: Lexington, MA, 445p.

NAL call number: QL813.C38D6 1989

Dissection manual illustrating cat anatomy and physiology.

Erlewein, D.L. and E.L. Kuhns (1996). *Instructions for Veterinary Clients: Canine and Feline Medical and Surgical Problems*. 3rd edition. Mosby: St. Louis, MO, 477p.

NAL call number: SF991.E75 1996

A notebook of instructions and information sheets veterinarians may provide to clients. Covers system disorders, parasitism, poisoning, nutrition, surgery, and miscellaneous conditions like acupuncture and cryotherapy.

- Ettinger, S.J. and E.C. Feldman (1995). *Textbook of Veterinary Internal Medicine: Diseases of the Dog and Cat*. 4th edition. W.B. Saunders: Philadelphia, 2 vol.  
NAL call number: SF991.T48 1995  
Covers clinical disease, systemic problems, infectious diseases, congenital defects, continuous rate infusion formulas, diagnosis, and treatment.
- Hudson, L.C. and W.P. Hamilton, eds. (1993). *Atlas of Feline Anatomy for Veterinarians*. Saunders:Philadelphia, PA, 287p.  
NAL call number: SF767.C29H83 1993  
Contains chapters on physical examinations and organ systems with illustrations.
- Institute of Laboratory Animal Resources Committee on Dogs (1994). *Dogs: Laboratory Animal Management*. National Academy Press: Washington, D.C., 138p.  
NAL call number: SF407.D6D64 1994  
Chapters cover criteria for experimental animal selection, husbandry, breeding colony management, veterinary care, and special considerations including diseases and gene therapy.
- McGinnis, T. (1996). *The Well Cat Book: The Classic Comprehensive Handbook of Cat Care*. Random House, NY, 325p.  
NAL call number: SF447.M3455 1996  
Reviews anatomy, preventative medicine, diagnostic medicine, home medical care, breeding and reproduction, and the role of the veterinarian. Written for the cat owner.
- McGinnis, T. (1996). *The Well Dog Book: The Classic, Comprehensive Handbook of Dog Care*. Random House: NY, 287p.  
NAL call number: SF427.M473 1996  
Reviews anatomy, preventative medicine, diagnostic medicine, home medical care, breeding and reproduction, and the role of the veterinarian. Written for the dog owner.
- Schwartz, S. (1997). *Canine and Feline Behavior Problems: Instructions for Veterinary Clients*. 2nd edition. Mosby, St. Louis, 144p.  
NAL call number: SF433.S38 1997  
Covers behavioral problems dealing with elimination, aggression, reproduction, ingestion, neuroses and emotional reactions, destructiveness, disease, and miscellaneous topics.
- Sussman, L. and A. Dubowy (1994). *The American Animal Hospital Association Encyclopedia of Cat Health and Care*. Hearst Books: New York, 291p.  
NAL call number: SF447.S87 1994  
Basic care, behavior, vaccinations, and disease recognition and treatment. Covers conditions specific to puppies, males, females, first aid, emergency procedures, and poison control.
- Wills, J. and A. Wolf, eds. (1993). *Handbook of Feline Medicine*. 1st edition. Pergamon Press: Oxford; New York, NY, 415p.  
NAL call number: SF985.H36 1993  
Contains chapters on disorders, symptoms, and treatments.

## Diseases and Parasites

- Buergelt, C.D. (1997). *Color Atlas of Reproductive Pathology of Domestic Animals*. Mosby: St. Louis, MO, 219p.  
NAL call number: SF871 B83 1997  
Describes normal and abnormal reproductive pathological conditions in mammals with color and black and white plates.
- Carter, G.R. and M.M. Chengappa (1993). *Microbial Diseases: A Veterinarian's Guide to Laboratory Diagnosis*. 1st edition. Iowa State University Press: Ames, IA, 304p.  
NAL call number: SF781.C365 1993  
Diagnosis, treatment, and control of microbial diseases in farm and companion animal species.
- Fraser, C.M., ed. (1991). *The Merck Veterinary Manual*. 7th edition. Merck and Company: Rahway, NJ, 1832p.  
NAL call number: SF748.N47  
Comprehensive reference of current knowledge related to the diagnosis, treatment, toxicology, and pharmacology of domestic, exotic, and laboratory animals.
- Frye, F.L. (1994). *Reptile Clinician's Handbook: A Compact Clinical and Surgical Reference*. Krieger Publishing Co.: Malabar, FL, 276p.  
NAL call number: SF997.5 R4F796 1994  
Describes diseases and other conditions requiring diagnosis, treatment, and prevention. Includes nutrition, reproduction, restraint and transport, anesthesia, and fluid replacement are some of the subjects covered.
- Frye, F.L. and D.L. Williams (1995). *Self-assessment Color Review of Reptiles and Amphibians*. Iowa State University Press: Ames, IA, 192p.  
NAL call number: SF997.5 R4F797 1995  
Color plates useful in identifying disease conditions in reptiles and amphibians.
- Jubb, K.V.F., P.C. Kennedy, and N. Palmer (1993). *Pathology of Domestic Animals*. 3rd edition. Academic Press: San Diego, CA, 3 volumes.  
NAL call number: SF769.J82  
Coverage of the pathology of diseases that infect tissues and organ systems.
- Harkness, J.E. and J.E. Wagner (1995). *The Biology and Medicine of Rabbits and Rodents*. 4th edition. Williams & Wilkens: Baltimore, MD, 372p.  
NAL call number: SF996.5.H37 1995  
Describes the biology and husbandry of the species, clinical procedures, diagnosis, specific conditions, and case reports.
- McEntee (1990). *Reproductive Pathology of Domestic Mammals*. Academic Press: San Diego, 401p.  
NAL call number: SF871.M3.



Useful to veterinary students, teachers, researchers, veterinarians, and pathologists. Contains comprehensive coverage of normal and abnormal anatomy and pathology of domestic mammalian reproductive systems.

Owen, D.G. (1992). *Parasites of Laboratory Animals*. Royal Society of Medicine Services: London, 170p.

NAL call number: SF996.5.O94 1992

Published for Laboratory Animals, Ltd., this is Laboratory Animal Handbooks; no. 12 which covers parasites typically found in laboratory animals and their treatment.

Sodikoff, C. (1995). *Laboratory Profiles of Small Animal Diseases: A Guide to Laboratory Diagnosis*. 2nd edition. Mosby: St. Louis, MO, 435p.

NAL call number: SF991.S598 1995

Focus is on dog and cat diseases.

Urquhart, G.M., J. Armour, J.L. Duncan, A.M. Dunn and F.W. Jennings (1996). *Veterinary Parasitology*. 2nd edition. Blackwell Scientific: Cambridge, MA, 307p.

NAL call number: SF810 A3V425 1996

Covers helminthology, entomology, and protozoology of domestic species. Intended for those involved in the diagnosis, treatment and control of parasitic diseases.

## **Ectotherms (Amphibians, Fish, Reptiles)**

DeNardo, D. (1995). **Amphibians as laboratory animals**. *ILAR Journal* 37(4):173-181.

NAL call number: QL55.A1I43

Information on housing, husbandry, water quality, anesthesia, euthanasia, and surgery of amphibians.

DeTolla, L.J., S. Srinivas, B.R. Whitaker, C. Andrews, B. Hecker, A.S. Kane, and R. Reimschuessel (1995). **Guidelines for the Care and Use of Fish in Research**. *ILAR Journal* 37(4):159-173.

NAL call number: QL55.A1I43

Covers husbandry, anesthesia, zoonoses, euthanasia, regulations, and fish use in biomedical research.

Frye, F.L. (1991). *Biomedical and Surgical Aspects of Captive Reptile Husbandry*. 2nd edition. Krieger Publishing Co.: Malabar, FL, 2 vol.

NAL call number: SF997.5.R4F78 1991 Fo

Covers diseases and surgery. Well-illustrated with color plates.

Frye, F.L. (1991). *A Practical Guide for Feeding Captive Reptiles*. Krieger Publishing Co.: Malabar, FL, 171p.

NAL call number: SF515.F79 1991

Diet composition and methods of feeding reptiles.

- Frye, F.L. (1991). *Reptile Care: An Atlas of Diseases and Treatments*. T.F.H. Publications: Neptune City, NJ, 2 vol.  
NAL call number: SF997.5.R4F795 1991 Fo  
Some of the topics covered include husbandry, radiology, ophthalmic conditions, reproductive disorders, bacterial and fungal diseases, surgery, histology, anesthesia, euthanasia and necropsy, use of antibiotics, and hematology.
- Messonnier, S.P. (1996). *Common Reptile Diseases and Treatment*. Blackwell Science: Cambridge, MA, 174p.  
NAL call number: SF997.5.P4M47 1996  
Briefly covers housing, feeding, and starting a reptile practice. More extensive information is provided on clinical procedures, diseases and treatments, and parasites in snakes, turtles, and iguanas. Appendices give specific treatment protocols, list of supplies, and normal blood values.
- Schaeffer, D.O., K.M. Kleinow, and L. Krulisch, eds. (1992). *The Care and Use of Amphibians, Reptiles and Fish in Research*. Scientists Center for Animal Welfare: Greenbelt, MD, 196p.  
NAL call number: SF406 C5 1992  
Conference proceedings covers housing, handling, nutrition, regulations and guidelines, and medicine of reptiles, amphibians, and fish.
- Warwick, C., F.L. Frye, and J.B. Murphy, eds. (1995). *Health and Welfare of Captive Reptiles*. Chapman & Hall: London; New York, 299p.  
NAL call number: SF515.H43 1995  
Chapters cover physiology, anatomy, stress, nutrition, veterinary perspectives, husbandry, housing, immunology, metabolism, reproduction, and welfare of reptiles in zoos, laboratories, and by pet owners.

## Formularies

- Bishop, Y.M. (1996). *The Veterinary formulary : Handbook of Medicines Used in Veterinary Practice*. 3rd edition. Rittenhouse: King of Prussia, PA [distributor], 513p.  
NAL call number: SF916.5.V47 1996  
Contains 1800 formulations of 700 drugs including abamectin, aciclovir, cefquinome, chlamydiosis vaccine, diazinon, doramectin, marbofloxacin, moxidectin, and pigeon pox vaccine. There is a section on prescribing for fish. Also included are drugs used in the treatment and control of parasitic infections.
- Borchard, R.E., C.D. Barnes, and L.G.Eltherington (1990). *Drug Dosage in Laboratory Animals: A Handbook*. 3rd edition. Telford Press: Caldwell, NJ, 692p.  
NAL call number: RM145.B65 1990  
Includes types of anesthesia and analgesia, their advantages and disadvantages, drug dosage tables, hormone maintenance and replacement dosage, and physiological solutions.

- Debuf, Y.M. (1994). *The Veterinary Formulary: Handbook of Medicines Used in Veterinary Practice*. 2nd edition. Pharmaceutical Press: London; King of Prussia: Rittenhouse [distributor], PA, 460p.  
NAL call number: SF917.V48 1994  
Prepared in the Department of Pharmaceutical Sciences of the Royal Pharmaceutical Society of Great Britain. Dosages of drugs for fish, reptiles, domestic and exotic animals, and invertebrates. 1650 drugs and dosages including auranofin, baquiloprim, bisacodyl, carprofen, ceftiofur, diclazuril, enalapril, enrofloxacin, epirubicin, famotidine, fluorometholone, gamolinolenic acid, isotretinoin, lufenuron, meloxicam, mesalazine, midazolam, misoprostol, mitozantrone, nalbuphine, olsalazine, omeprazole, phenylpropanolamine, romifidine and tilmicosin, and other drugs. Mention of proprietary preparations from 164 manufacturers or distributors.
- Hawk, C.T. and S.L. Leary (1995). *Formulary for Laboratory Animals*. Iowa State University Press: Ames, IA, 101p.  
NAL call number: SF917.H25 1995  
A guide sponsored by the American College of Laboratory Animal Medicine provides dosages of analgesics, anesthetics, anti-infective agents, parasiticides and other drugs for 21 groups of laboratory animals. Dosage data is linked to literature references. The appendices summarize bleeding sites, blood volumes, endotracheal tubes, needle sizes and the toxicity of antibiotics for rodents and rabbits.
- Knott, T.A. (1997). *Formulary of Equine Medicine*. 3rd edition. Liverpool University Press: Liverpool, U.K., 340p.  
NAL call number: SF951.F67 1997  
Describes veterinary medicine, disease, and drug dosages in horses.
- Lucotte, G. (1993). *Genetic Engineering Formulary. (Formulaire de Genie Genetique)*. Technique et Documentation Lavoisier: Paris; France, 107p.  
Data on the biological or physico-chemical characteristics of restriction enzymes, reagents, vectors, Escherichia coli strains, culture media, antibiotics and techniques used in cloning and DNA hybridization.
- Marx, K.L. and M.A. Roston (1996). *The Exotic Animal Drug Compendium: An International Formulary*. Veterinary Learning Systems: Trenton, NJ, 393p.  
NAL call number: SF917.M37 1996  
Contains 740 compounds, including dosage, administration, and references, are given for all groups of vertebrate animals. They include analgesia, anesthesia, antibacterial agents, anticonvulsants. Generic and proprietary names are given.
- Tennant, B. (1994). *Small Animal Formulary*. British Small Animal Veterinary Association: Cheltenham, Gloucs, U.K., 218p.  
NAL call number: SF917.T46 1994  
Lists drugs with indications, forms, interactions, dosages, adverse effects, and contraindications. Useful for animal care staff and students.

## General Laboratory Animal Care and Use

- Appleby, M. and B.O. Hughes, eds. (1997). *Animal Welfare*. CAB International: Oxon, U.K. and New York, 316p.  
NAL call number: HV4711 A587 1997  
Reviews issues, problems, and assessments, and solutions in animal welfare from ethical and scientific perspectives. Some of the topics cover include pain and injury; fear and distress; hunger and thirst; health and disease; behavior; physiology; social conditions; human contact; economics; and legislation.
- Bennett, B.T., M.J. Brown, and J.C. Schofield, eds. (1994). *Essentials for Animal Research: A Primer for Research Personnel*. 2nd edition. Animal Welfare Information Center, National Agricultural Library: Beltsville, MD and University of Illinois at Chicago: Chicago, IL, 84p.  
NAL call number: aQL55 B36 1994  
Provides an overview of animal use regulations, alternatives, pain relief, euthanasia, surgery, and the services of the Animal Welfare Information Center.
- Claassen, V. (1994). *Neglected Factors in Pharmacology and Neuroscience Research: Biopharmaceutics, Animal Characteristics, Maintenance, Testing Conditions*. Elsevier: Amsterdam, New York, Oxford, 486p.  
NAL call number: RM301.25.c56 1994  
Seventeen chapters detail drug administration; strain, sex, and age aspects of animals; housing and nutrition; experimental conditions such as feed restriction, fasting, and circadian rhythms; anesthesia; and stress.
- Foundation for Biomedical Research (1987). *The Biomedical Investigator's Handbook for Researchers Using Animal Models*. Foundation for Biomedical Research: Washington, DC, 86p.  
NAL call number: QL55 B5  
The first part of this document describes how to comply with Federal animal care regulations, euthanasia, complicating factors in animal care, biological hazards in the laboratory, good surgical practices, and research oversight. The second part describes how researchers should defend animal research and create good public relations in response to animal rights citizens critical of animal research.
- Hitzelberg, R., E. Lundgren, and J. Phillips, eds. (1987). *Laboratory Manual for Basic Bi methodology of Laboratory Animals*. MTM Associates, Inc.: Silver Spring, MD.  
NAL call number: SF406.H5 vol.1 and vol.2.  
The first volume contains information on mice, rats, guinea pigs and rabbits; and the second on dogs, cats and primates. Methods for restraint, injection routes, blood collection, and euthanasia are covered for each species.
- Hrapkiewicz, K., L. Medina, and D.D. Holmes (1998). *Clinical Laboratory Animal Medicine*. 2nd edition. Iowa State University Press: Ames, IA, 277p.  
NAL call number: SF996.5.H65 1998



Species include mice, rats, gerbils, hamsters, guinea pigs, chinchillas, rabbits, ferrets, and nonhuman primates. Each chapter covers housing, husbandry, diseases, surgical and handling techniques, euthanasia, therapeutic agents, and fluid collection. Also includes chapters on serologic testing and quality control, regulations and policies about animal care and use, organizations in laboratory animal medicine, and appendices with normal values.

National Research Council Committee on Educational Programs in Laboratory Animal Science (1991). *Education and Training in the Care and Use of Laboratory Animals: A Guide for Developing Institutional Programs*. National Academy Press: Washington, D.C., 139p.  
NAL call number: SF604.E3

In response to Animal Welfare Act and Health Research Extension Act mandates for institutions to provide training to animal care and use staff, the Institute for Laboratory Animal Resources (ILAR) established a committee to develop this training manual. The manual contains ten course modules, a resources section, and instructions on developing and evaluating educational programs. The modules cover legislation and policies, ethical and scientific issues, alternatives, animal care and use committees, pain and distress, pain relief, surgery, euthanasia, husbandry, and species-specific overviews.

Olfert, E.D., B.M. Cross, and A.A. McWilliam, eds. (1993, 1984). *Guide to the Care and Use of Experimental Animals*. 2 Volumes. Canadian Council on Animal Care: Ontario, Canada. Copies available from: CCAC, 1000-151 Slater Street, Ottawa, Ontario K1P 5H3. Vol. 1, 2nd. edition, 218p. Vol. 2, 208p.  
NAL call number Vol. 1: SF406 G85 1993  
NAL call number Vol. 2: SF406 C36

A reference guide for the humane care and use of animals used in research, teaching, and testing. Volume 1 includes a discussion of the Canadian oversight committee system, laboratory and farm animal facilities, the environment, animal care, social and behavioral requirements of animals, restraint, occupational health and safety, pain control, euthanasia, zoonoses and other diseases, drug dosages, and CCAC position statements. Volume 2 contains species-specific care chapters. Traditional laboratory and farm species are covered as are fish, reptiles, amphibians, and wild vertebrates in the field.

Poole, T.B., ed. (1987). *The UFAW Handbook on the Care and Use of Laboratory Animals*. 6th edition (7th edition due 1998). Longman Scientific and Technical: London, UK, Churchill Livingstone, Inc.: New York, NY, 918p.  
NAL call number: QL55 U5 1987

Various authors cover housing, husbandry, and experimental techniques for marsupials, bats, armadillos, rodents, rabbits, ferrets, dogs, cats, farm animals, nonhuman primates including shrews, birds, reptiles, amphibians, and fish.

Pratt, P.W. (1997). *Laboratory Procedures for Veterinary Technicians*. 3rd edition. Mosby: St. Louis, MO, 601p.  
NAL call number: SF772.6 L32 1997  
Covers all aspects of laboratory procedures for laboratory technicians.

Stark, D.M. and M.E. Ostrow, eds. (1989). *AALAS Training Manual Series Volume 1: Assistant Laboratory Animal Technician*. American Association for Laboratory Animal Science: Cordova, TN, 186p.

NAL call number: SF406 A79 1989

Laboratory training manual covers scientific terminology, basic animal anatomy and physiology, and common laboratory instrumentation. Common laboratory procedures, housing requirements, and restraint and handling techniques are discussed for typical laboratory species.

Stark, D.M. and M.E. Ostrow, eds. (1990). *AALAS Training Manual Series Volume 2: Laboratory Animal Technician*. American Association for Laboratory Animal Science: Cordova, TN, 214p.

NAL call number: SF77 L25

This volume covers some of the topics in Volume 1, but in more depth. It includes discussions of standard procedures related to management, health, basic science, and husbandry of many of the less common laboratory animal species, such as the amphibians and reptiles. Equipment related to experimental and surgical procedures is also covered.

Stark, D.M. and M.E. Ostrow, eds. (1991). *AALAS Training Manual Series Volume 3: Laboratory Animal Technologist*. American Association for Laboratory Animal Science: Cordova, TN, 208p.

NAL call number: SF77 L26

Covers management and supervision, diagnostics, laboratory animal diseases, nutrition, equipment, anatomy, physiology, and experimental techniques. The AALAS series is designed to assist laboratory animal technical personnel prepare for certification examinations.

## Genetics and Transgenics

Hedrich, H.J. and M. Adams (1990). *Genetic Monitoring of Inbred Strains of Rats: A Manual on Colony Management, Basic Monitoring Techniques, and Genetic Variants of the Laboratory Rat*. Gustav Fischer Verlag: Stuttgart and New York, NY, 539p.

NAL call number: SF407.R38G46

Produced for the International Council for Laboratory Animal Science.

Kriegler, M. (1990). *Gene Transfer and Expression: A Laboratory Manual*. Stockton Press: New York, NY, 242p.

NAL call number: QH442.K73 1990

Covers DNA sequence project management, proteins, similarity and homology, practical aspects, and analysis.

Lucotte, G. (1993). *Genetic Engineering Formulary. (Formulaire de Genie Genetique)*.

Technique et Documentation Lavoisier: Paris; France, 107p.

Data on the biological or physico-chemical characteristics of restriction enzymes, reagents, vectors, Escherichia coli strains, culture media, antibiotics and techniques used in cloning and DNA hybridization.

Pinkert, C.A. (1994). *Transgenic Animal Technology: A Laboratory Handbook*. Academic Press: San Diego, CA, 364p.

NAL call number: QH442.6.T69 1994

Describes methods used in transgenic research in farm and laboratory animals.

## **Invertebrates**

Abramson, C.I. (1990). *Invertebrate Learning: A Laboratory Manual and Source Book*. American Psychological Association: Washington, D.C., 100p.

NAL call number: QL364.2.A27 1990

Designed for high school and college animal behavior laboratories.

Boyle, P.R. (1991). *The UFAW Handbook on the Care and Management of Cephalopods in the Laboratory*. Universities Federation for Animal Welfare: Wheathampstead, Herts, U.K., 63p.

NAL call number: SF407.M37B68

Describes taxonomy, anatomy, housing, husbandry, and experimental techniques in squid, octopus, and nautilus.

Ingle, R.W. (1995). *The UFAW Handbook on the Care and Management of Decapod Crustaceans in Captivity*. Universities Federation for Animal Welfare: Wheathampstead, Herts, U.K., 119p.

NAL call number: SF407 M37I54 1995

Covers the biology, management, rearing, feeding, collecting, handling and restraint, transport, anesthesia, euthanasia, and diseases.

National Research Council. Committee on Marine Invertebrates (1981). *Marine Invertebrates: Laboratory Animal Management*. National Academy Press: Washington, D.C., 382p.

NAL call number: SF407.M37M37

Methods for maintaining and rearing marine invertebrates in the laboratory without immediate access to the sea. Part one contains general information, while part two contains information on specific animals or groups of animals such as sea anemones, mollusks, annelids, crabs, sea urchins. Covers animal care, handling, and food requirements.

## **Laboratory Animal Housing**

Olfert, E.D., B.M. Cross, and A.A. McWilliam, eds. (1993, 1984). *Guide to the Care and Use of Experimental Animals*. 2 Volumes. Canadian Council on Animal Care: Ontario, Canada. Copies available from: CCAC, 1000-151 Slater Street, Ottawa, Ontario K1P 5H3. Vol. 1, 2nd. edition, 218p. Vol. 2, 208p.

NAL call number Vol. 1: SF406 G85 1993

NAL call number Vol. 2: SF406 C36

A reference guide for the humane care and use of animals used in research, teaching, and testing. Volume 1 includes a discussion of the Canadian oversight committee system, laboratory and farm animal facilities, the environment, animal care, social and behavioral requirements of animals, restraint, occupational health and safety, pain control, euthanasia,

zoonoses and other diseases, drug dosages, and CCAC position statements. Volume 2 contains species-specific care chapters. Traditional laboratory and farm species are covered as are fish, reptiles, amphibians, and wild vertebrates in the field.

Poole, T.B., ed. (1987). *The UFAW Handbook on the Care and Use of Laboratory Animals*. 6th edition (7th edition due 1998). Longman Scientific and Technical: London, UK, Churchill Livingstone, Inc.: New York, NY, 918p.

NAL call number: QL55 U5 1987

Various authors cover housing, husbandry, and experimental techniques for marsupials, bats, armadillos, rodents, rabbits, ferrets, dogs, cats, farm animals, nonhuman primates including shrews, birds, reptiles, amphibians, and fish.

Reinhardt, V., ed. (1997). *Comfortable Quarters for Laboratory Animals*. 8th edition. Animal Welfare Institute: Washington, DC, 115p.

NAL call number: SF91.A5

Includes guidelines and references for housing, handling, and environmental enrichment for rodents, reptiles and amphibians, chickens, rabbits, cats, dogs, nonhuman primates, sheep and goats, cattle, and swine.

## Legislation, Policies, and Guidelines

### General References:

Abbot, S.G. and L.W. Oring (1997). *Guidelines to the Use of Wild Birds in Research*. Special Publication. Ornithological Council: Washington, DC, 52p.

NAL call number: QL677.5.G75 1997

Professional guidelines for studies of wild birds in field and laboratory research. Covers permits, investigator impact, collecting and trapping, marking, transport, housing, minor manipulative procedures, and major manipulative procedures including surgery and euthanasia.

Animal Welfare Institute (1990). *Animals and Their Legal Rights: A Survey of American Laws from 1641 to 1990*. 4th edition. Animal Welfare Institute: Washington, DC, 441p.

NAL call number: HV4725 U5L4

An excellent review of laws and policies, their histories, and their enforcement. Individually authored chapters include humane slaughter laws, laboratory animal welfare, animals and airlines, dogs, cats, horses, fighting and baiting, trapping and poisoning, marine mammals, birds, nonhuman primates, humane education, international animal protection, and animal protective organizations and law enforcement agencies. Appendices include the text of mentioned laws.

Cooper, M.E. (1987). *An Introduction to Animal Law*. Academic Press, Inc.: Orlando, FL, 213p.

NAL call number: K3620.C58.

This book provides guidelines for those who wish to be pointed in the right direction but not to be overwhelmed by the details of law as it relates to animals.



## **Animal Welfare Act and Amendments:**

Animal Welfare Act, amendments, and regulations are available from USDA, APHIS, Office of Animal Care, 4700 River Rd., Unit 85, Riverdale, MD 20737-1234 and at <http://www.usda.gov/reac/>

### *Animal Welfare Act as Amended (7 U.S.Code, 2131-2156)*

The complete Animal Welfare Act including all amendments following the 1966 enactment.

### *Public Law 89-544 Act of August 24, 1966*

Referred to as *The Animal Welfare Act* although that title is not mentioned within the law. It authorizes the Secretary of Agriculture to regulate transport, sale, and handling of dogs, cats, nonhuman primates, guinea pigs, hamsters, and rabbits intended to be used in research or "for other purposes". It requires licensing and inspection of dog and cat dealers and humane handling at auction sales.

### *Public Law 91-579 Animal Welfare Act of 1970*

Expands the list of animals covered by the Act to include all warm-blooded animals determined by the Secretary of Agriculture as being used or intended for use in experimentation or exhibition except horses not used in research and farm animals used in production-related studies. Exhibitors are incorporated into the act and research facilities are defined. Retail pet stores, state and county fairs, rodeos, purebred dog and cat shows, and agricultural exhibitions are exempt from the act. The Secretary is directed to develop regulations regarding record keeping and humane care and treatment of animals in or during commerce, exhibition, experimentation, and transport. There is also mention of inspections, and appropriate anesthetics, analgesics, and tranquilizers. There are further regulations on dog and cat commerce.

### *Public Law 94-279 Animal Welfare Act Amendments of 1976*

Focuses on animal transport and commerce. Health certification prior to transport of sale is required and must be performed by a veterinarian. Licenses, method of payment, and penalties for violations are discussed. This amendment also introduces and defines "animal fighting ventures" to the Act. Animals used in hunting waterfowl, foxes, etc. are exempt. It is illegal to exhibit or transport via interstate or foreign commerce animals used in fighting ventures such as dogs or roosters.

### *Public Law 99-198 Food Security Act of 1985, Subtitle F - Animal Welfare*

Also called "The Improved Laboratory Standards Act", this section clarifies what is meant by "humane care" by mentioning specifics such as sanitation, housing, and ventilation. It directs the Secretary of Agriculture to establish regulations to provide exercise for dogs and an adequate physical environment to promote the psychological well-being of nonhuman primates. It specifies that pain and distress must be minimized in experimental procedures and that alternatives to such procedures be considered by the principle investigator. It also defines practices that are considered to be painful. No animal can be used in more than one major operative experiment with recovery (exceptions are listed). The establishment of the Institutional Animal Care and Use Committee (IACUC) is introduced with a description of its roles, composition, and responsibilities to the Animal and Plant Health Inspection Service (APHIS). Also included is the formation of an information service at the National Agricultural Library to assist those regulated by the act in prevention of unintended duplication of research, employee training, searching for ways to reduce or replace animal use, and to provide information on how to decrease pain and distress. The final section explains the penalties for release of trade secrets by regulators and the regulated community.

Public Law 101-624 *Food, Agriculture, Conservation, and Trade Act of 1990, Section 2503 - Protection of Pets*

Establishes a holding period for dogs and cats at shelters and other holding facilities before sale to dealers. It requires dealers to provide written certification regarding each animal's background to the recipient. Specific items included on the certificate are mechanisms of enforcement, injunctions, and penalties for violation.

*Code of Federal Regulations, Title 9, Chapter 1, Subchapter A - Animal Welfare*

Commonly called "9CFR", the regulations developed by the U.S. Department of Agriculture describe how the Act and Amendments must be implemented. The Definitions section describes exactly what is meant by terms used in the legislation. "Animal", for example, specifically excludes rats of the genus *Rattus* and mice of the genus *Mus* as well as birds used in research. The Regulations section includes subparts for licensing, registration, research facilities, attending veterinarians and adequate veterinary care, stolen animals, records, compliance with standards and holding periods, and miscellaneous topics such as confiscation and destruction of animals and access and inspection of records and property. The bulk of the 9CFR subchapter is the third section which provides standards for specific species or groups of species. Included are sections for cats and dogs, guinea pigs and hamsters, rabbits, nonhuman primates, marine mammals, and the general category of "other warm-blooded animals". Standards include those for facilities and operations, health and husbandry systems, and transportation. The final section sets forth the Rules of Practice applicable to adjudicating administrative proceedings under Section 19 of the Animal Welfare Act. This is the 1994 version of the Code of Federal Regulations.

*Federal Register*, Vol. 54, No. 168, August 31, 1989, P. 36112-36163. *Final Rule: Animal Welfare; Parts 1, 2, and 3.*

The final regulations developed to enact the 1985 amendments to the Animal Welfare Act. Extensive commentary is provided to respond to public comments about each of the proposed regulations. Often referred to as the "Preamble" to the Animal Welfare Act amendments of 1985, the explanations of the regulations are used to identify the intent of the regulations published in *Title 9, Code of Federal Regulations*.

*Federal Register*, Vol. 55, No. 32, February 15, 1991, P. 6426-6505. *Final Rule: Animal Welfare; Standards; Part 3.*

The final regulations developed to enact the 1985 amendments to the Animal Welfare Act concerning exercise in dogs and psychological well-being in nonhuman primates. Extensive commentary is provided to respond to public comments about each of the proposed regulations. Also referred to as the "Preamble" to the Animal Welfare Act amendments of 1985, the explanations of the regulations are used to identify the intent of the regulations published in 9CFR.

*Federal Register*, Vol. 58, No. 139, July 22, 1993, P. 39124. *Final Rule: Random Source Dogs and Cats*, and *Federal Register*, Vol. 58, No. 164, August 26, 1993, P. 45040. *Final Rule: Correction, Random Source Dogs and Cats.*

The final rules amending the regulations under the Animal Welfare Act requiring pounds and shelters to hold and care for dogs and cats for at least 5 days (including one weekend day) before providing them to a dealer. Dealers must provide valid certification to anyone acquiring random source dogs and cats from them. Public comments and rationale for the regulatory decisions are discussed.

## National Institutes of Health Legislation, Policies, and Guidelines:

Available from Office for Protection from Research Risks, Division of Animal Welfare, 6100 Executive Blvd., Suite B01, Rockville, MD 20892-7505 and from [http://www.nih.gov:80/grants/oprr/library\\_animal.htm](http://www.nih.gov:80/grants/oprr/library_animal.htm)

National Research Council, Institute of Laboratory Animal Resources (1996). *Guide for the Care and Use of Laboratory Animals*. National Academy Press: Washington, D.C., 127p. Also available electronically from [http://www.nih.gov:80/grants/oprr/library\\_animal.htm](http://www.nih.gov:80/grants/oprr/library_animal.htm)

NAL call number: SF406 G95 1996

Public Health Service grantees and contractors and AAALAC-accredited (Association for Assessment and Accreditation of Laboratory Animal Care International) facilities are required to abide by the Animal Welfare Act and amendments and the recommendations found in the *Guide* and the *PHS Policy*. The *Guide* includes minimum requirements and performance standards for institutional policies, laboratory animal husbandry, veterinary care, physical plant, and special considerations such as farm animals. Unlike the Animal Welfare Act, the guide is used for all animal species.

PL 99-158 *Health Research Extension Act of 1985, Section 495*

Section 495, "Animals in Research", requires the Secretary of the Public Health Service (PHS) to develop and implement regulations for the humane care and use of animals in research by institutions (including Federal facilities) that receive PHS funding. The complete law can be found in *U.S. Code, Title 42*.

Public Health Service (1996). *Public Health Service Policy on Humane Care and Use of Laboratory Animals*. 16p.

NAL call number: QL55 P82 1986

The *Policy* was established in accordance with the Health Research Extension Act of 1985 (PL 99-158). It must be used to supplement the Animal Welfare Act and amendments by PHS grantees and contractors. It includes policy on animal welfare assurance, composition and function of institutional animal care and use committees, information required to apply for PHS funding and review of research, record keeping and reporting requirements, and implementation by PHS.

Office for Protection from Research Risks. *OPRR Reports: "Dear Colleague Letters"*.

Letters that are published in *OPRR Reports* or mailed to PHS-funded institutions about OPRR policies. Topics include sources of antibody production, clarifications of reporting requirements, definitions and problems with expedited reviews, information about prompt reporting of problems, and the new addresses and phone numbers of OPRR personnel.

Editorial Committee of Institutional Administrators and Laboratory Animal Specialists for the Henry M. Jackson Foundation for Advancement of Military Medicine, Uniformed Services University of Health Sciences (1988). *Institutional Administrator's Manual for Laboratory Animal Care and Use*. Bethesda, MD: U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, 82p.

NAL call number: SF406 I54



A guide for institutional administrators who supervise laboratory animal care and use programs. The manual addresses questions involving quality care, ethics, and legal requirements for animal care and use programs.

ARENA (Applied Research Ethics National Association)(Updated version, 1994). *Institutional Animal Care and Use Committee Guidebook*. Available from: National Institutes of Health, Council of the Applied Research Ethics National Association (ARENA) (1992). *Institutional Animal Care and Use Committee Guidebook*. National Institutes of Health Publication No. 92-3415, National Institutes of Health: Bethesda, MD, 60p.

NAL call number: HV4764.I58 1992

Excellent overview of Institutional Animal Care and Use Committee composition, function, proposal review, oversight of the animal care and use program, record keeping, sample forms, and special considerations. Useful review of NIH policies and the Animal Welfare Act as they pertain to the committee.

### **Other legislation, policies, and guidelines:**

AVMA (American Veterinary Medical Association)(1993). **1993 Report of the AVMA Panel on Euthanasia**. *Journal of the American Veterinary Medical Association* 202:229-249.

NAL call number: 41.8 AM3

Recommendations for humane euthanasia of vertebrates including acceptable methods, mechanisms of action, and special considerations.

*Code of Federal Regulations, Title 21, Chapter 1, Part 58, Good Laboratory Practice for Nonclinical Laboratory Studies*. Available from: Office of Regulatory Affairs, Food and Drug Administration, 5600 Fisher Lane, Rockville, MD 20857.

Administered by the Food and Drug Administration, these regulations prescribe good laboratory practices for conducting nonclinical laboratory studies that support research or marketing permits for products regulated by the Food and Drug Administration. These including food and color additives, animal food additives, human and animal drugs, medical devices for human use, biological products, and electronic products. Companion regulations for conducting studies relating to health effects, environmental effects, and chemical fate testing are found in *Code of Federal Regulations, Title 40, Chapter 1, Part 792, Good Laboratory Practice Standards* and are administered by the Environmental Protection Agency.

*Code of Federal Regulations, Title 40, Chapter 1, Part 792, Good Laboratory Practice Standards*. Available from: Environmental Protection Agency, 401 M St. S.W., Washington, D.C. 20460.

In accordance with Section 4 of the Toxic Substances Control Act, the Environmental Protection Agency issued these regulations describing laboratory practices for conducting studies relating to health effects, environmental effects, and chemical fate testing. Companion regulations for product testing regulated by the Food and Drug Administration are found in *Title 21, Chapter 1, Part 58 - Good Laboratory Practice for Nonclinical Laboratory Studies*.

*Federal Register*, Volume 59, No. 127, Tuesday, July 5, 1994, P. 34496-34547.

*National Institutes of Health: Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines)*.



The NIH Guidelines specify practices for constructing and handling recombinant deoxyribonucleic acid (DNA) molecules and organisms and viruses containing recombinant DNA molecules. Includes topics such as biosafety, gene transfer, and institutional responsibilities.

*Federal Register, Volume 54, No. 75, Thursday, April 20, 1989, Good Laboratory Practice: Minor Amendment.* Available from: Office of Regulatory Affairs, Food and Drug Administration, 5600 Fisher Lane, Rockville, MD 20857.

The final rule discouraging toe clipping for laboratory animal identification is discussed as an amendment to the Food and Drug Administration's *Good Laboratory Practice Standards*.

*U.S. Code, Title 18, Public Law 102-346 Animal Enterprise Protection Act of 1992.*

Makes "physical disruption" of animal enterprises by property damage, theft, economic damage exceeding \$10,000, serious bodily injury or death a criminal offense. Resulted in a study conducted by the Attorney General and the Secretary of Agriculture on the extent and effects of terrorism on enterprises using animals for food and fiber production, agriculture, research, or testing and present their findings and recommendations to Congress.

Universities Federation for Animal Welfare (1990). *Guidelines on the Care of Laboratory Animals IV. Planning and Design of Experiments.* Universities Federation for Animal Welfare: Wheathampstead, Herts, U.K., 22p.

## Medical and Veterinary Dictionaries

Dorland, W.A.N. (1994). *Dorland's Illustrated Medical Dictionary.* 28th edition. Saunders: Philadelphia, PA, 1940p.

NAL call number: R121.D73 1994

Covers anatomy, genetics, diseases, reference values for laboratory tests, tables of culture media, physiology, biochemistry, and selected abbreviations used in medicine.

Frenay, A.C. and R.M. Mahoney (1989). *Understanding Medical Terminology.* 8th edition.

Kendall/Hunt Publishing Co.: Dubuque, IA.

NAL call number: R123.F7.

An illustrated guide explaining biomedical terminology.

Ilchmann, G. and T. Blaha (1993). *Dictionary of Veterinary Medicine.* A. Hatier: Berlin, Germany, 414p.

NAL call number SF609.F32 1993

Veterinary terms from parasitology, pathology, pharmacology, epidemiology, animal and food hygiene in German, English, French, and Russian.

Jablonski, S. (1993). *Dictionary of Medical Acronyms and Abbreviations.* 2nd edition. Hanley & Belfus: Philadelphia, PA, 330p.

NAL call number: R123 J24 1993

McBride, D.F. and M.G. Austrin (1996). *Learning Veterinary Terminology.* Mosby: St. Louis, MO, 541p.

NAL call number: SF610.M38 1996

Four sections describe the basic foundation of veterinary language, body structure and systems, and animal industry terms.

Parker, S.P. (1994). *McGraw-Hill Dictionary of Scientific and Technical Terms*. 5th edition. McGraw-Hill: New York, NY, 2194p.  
NAL call number: Q193.M15 1994

Parker, S.P. (1994). *McGraw-Hill Concise Encyclopedia of Science & Technology*. 3rd edition. McGraw-Hill: New York, NY, 2241p.  
NAL call number Q121.M29 1994  
This volume is condensed from a 15-volume set.

Stanfield, P. and Y.H. Hui (1991). *Essential Medical Terminology*. Jones and Bartlett: Boston, MA, 287p.  
NAL call number R123.S678-1991  
Contains comprehensive coverage of over 1,400 medical terms, hundreds of exercises and progress checks with answers, and full-color anatomical art work.

Thomas, C.L., ed. (1990). *Taber's Cyclopedic Medical Dictionary*. 16th edition. F.A. Davis Co.: Philadelphia, PA.  
NAL call number: R121.T144.  
A dictionary of medical terminology.

West, G., ed. (1988). *Black's Veterinary Dictionary*. 16th edition. Barnes & Noble Books: Totowa, NJ.  
NAL call number: SF609.M5.  
An illustrated dictionary containing information on animal anatomy, physiology, diseases, medicine, and research.

Wiesner, E. and Eikmeier, H. (1991). *Concise Dictionary of Veterinary Practice*. G. Fischer: New York: NY.  
NAL call number: SF609.H36 1991  
A five-volume set covering many facets of veterinary practice. Written in German.

## Occupational Safety

Institute of Laboratory Animal Resources (U.S.). Committee on Occupational Safety and Health in Research Animal Facilities (1997). *Occupational Health and Safety in the Care and Use of Research Animals*. National Academy Press: Washington, DC, 154p.  
NAL call number: RC965.A6O23 1997

Richmond, J.Y. and R.W. McKinney, eds. (1993). 3rd edition. *Biosafety in Microbiological and Biomedical Laboratories*. HHS Publication No. (CDC) 93-8395. U.S. Government Printing Office: Washington, D.C., 177p.

NAL call number: Q183 B56 1993

This publication is issued by Centers for Disease Control and Prevention and the National Institutes of Health. Includes sections on biosafety principles, level criteria, levels for infectious agents and infected animals, risk assessment, types of agents, appendices, and a list of resources.

## Philosophy and Ethics

American Medical Association (1988). *Use of Animals in Biomedical Research: The Challenge and Response*. American Medical Association: Chicago, IL, 36p.

NAL call number: HV4932.U73.

An AMA White Paper that presents a concise overview of the pro-animal research perspective including background on the animal rights movement and justification for animal research.

Anderson, D.; M.J. Reiss; and P.N. Campbell, eds. (1993). *Ethical Issues in Biomedical Sciences: Animals in Research and Education*. Institute of Biology: London, UK, 103p.

NAL call number: HV4913.E84 1993

Proceedings of a National conference organized by the Institute of Biology's Biomedical Sciences and Education Divisional Committees in collaboration with the British Toxicology Society held in London, October 1992.

Appleby, M. and B.O. Hughes, eds. (1997). *Animal Welfare*. CAB International: Oxon, U.K. and New York, 316p.

NAL call number: HV4711 A587 1997

Reviews issues, problems, and assessments, and solutions in animal welfare from ethical and scientific perspectives. Some of the topics cover include pain and injury; fear and distress; hunger and thirst; health and disease; behavior; physiology; social conditions; human contact; economics; and legislation.

Baird, R.M. and S.E. Rosenbaum (1991). *Animal Experimentation: The Moral Issues*. Prometheus Books: Buffalo, N.Y., 182p.

NAL call number: HV4915.A64

Beauchamp, T.L. and L. Walters, eds. (1989). *Contemporary Issues in Bioethics*. 3rd edition. Wadsworth Publishing Company: Belmont, CA.

NAL call number: R724.C67

Focuses on moral perplexities in biomedical research. The objective of this book is to make students aware of complex situations in biology and medicine that require moral reflection, judgement, or decision. The essays have been arranged in a debate-like format, with divergent viewpoints placed side-by-side, so that the reader can explore the strengths and weaknesses of alternative positions.

Bekoff, M. and C.A. Meaney, eds. (1998). *Encyclopedia of Animal Rights and Animal Welfare*. Greenwood Press: Westport, CT.

Geared towards the general public and students, this comprehensive encyclopedia briefly covers everything from animals in religion to euthanasia. Each topic is addressed by an

expert in that area. Pain, distress, legislation, philosophy, and animal shelters are also covered. An concise introduction to the field.

Blum, D. (1994). *The Monkey Wars*. Oxford University Press: New York, NY, 306p.

NAL call number: HV4915 B58 1994

Written by a journalist, this book carefully examines the viewpoints of researchers who study nonhuman primates and those who strongly oppose such research. The author a historical background, the arguments, and very balanced interviews and discussion of research benefits and flaws.

Committee on the Use of Animals in Research (1991). *Science, Medicine, and Animals*. National Academy Press: Washington, DC, 30p.

NAL call number: HV4915 S35

Prepared for the Councils of the National Academy of Sciences and the Institute of Medicine by the Committee on the Use of Animals in Research, this document seeks to answer the most commonly asked questions about animal research, and to describe some of the ways in which animal research has benefitted, and continues to benefit, human and animal health.

Dawkins, M.S. and M. Gosling (1992). *Ethics in Research on Animal Behaviour: Readings from Animal Behaviour*. Academic Press for the Association for the Study of Animal Behaviour and the Animal Behavior Society: London, England, 64p.

NAL call number: QL55.E84-1992

Includes "Guidelines for the Use of Animals in Research," revised 1991 version.

Deyn, P.P. de; R. D'Hooge; and A. Schafer (1994). *The Ethics of Animal and Human Experimentation*. John Libbey: London, 369p.

NAL call number: HV4915.E84 1994

General reflections and considerations in regard to biomedical science, legislation, European guidelines, and controversies involving human or non-human subjects used in research.

Groves, J.M. (1997). *Hearts and Minds: The Controversy Over Laboratory Animals*. Temple University Press: Philadelphia, PA, 230p.

NAL call number: R853.A53G76 1997

A look at ethics practiced in the everyday lives of animal researchers and animal rights advocates. Why and how people deal with animal issues at sociological and psychological levels are discussed.

Harnack, A. (1996). *Animal Rights: Opposing Viewpoints*. Greenhaven Press: San Diego, CA, 240p.

NAL call number: HV4711.A58 1996

Asks similar questions as the first edition (1989), but uses different, more recent, articles in reply. Pro and con cases are made for animal rights, experimentation, wildlife protection, animals as food, and others.

LaFollette, H. and N. Shanks (1996). *Brute Science: Dilemmas of Animal Experimentation*.

Routledge: London, New York, 286p.

NAL call number: HV4915.L34 1996

An analysis of philosophy and morality of animal experimentation.



Orlans, F.B. , T.L. Beauchamp, R. Dresser, D.B. Morton, and J.P. Gluck (1998). *The Human Use of Animals: Case Studies in Ethical Choice*. Oxford University Press: Oxford, New York, 330p.

This book covers 16 case studies about ethical issues in human-animal interactions. Topics addressed include biomedical research, cosmetic safety testing, behavioral research, wildlife research, educational teaching, food and farming, companion animals, and religious rites.

Orlans, F.B. (1993). *In the Name of Science: Issues in Responsible Animal Experimentation*. Oxford University Press: New York, NY, 297p.

NAL call number: HV4915.O75 1993

Addresses attitudes and ethical arguments, alternatives, IACUCs, protocol reviews, pain and suffering, testing, animals in education, and makes recommendations for policy changes.

Phillips, M.T. and J.A. Sechzer (1989). *Animal Research and Ethical Conflict: An Analysis of the Scientific Literature, 1966-1986*. Springer-Verlag: New York, 251p.

NAL call number: HV4708.P55

A survey of the scientific literature addressing ethical and humane issues of animal research.

Regan, T. and P. Singer, eds. (1989). *Animal Rights and Human Obligations*. 2nd edition. Prentice Hall: Englewood Cliffs, NJ, 280p.

NAL call number: HV4711.A56 1989

Discusses animal rights, humaneness, morality, and ethical animal use by man.

Rohr, J., ed. (1989). *Animal Rights: Opposing Viewpoints*. Greenhaven Press, Inc.: San Diego, CA  
NAL call number: HV4711.A53.

Geared towards students, this book presents excerpts from articles by well-known philosophers and scientists that present pro- and con- views about whether animals have rights. Opposing viewpoints are expressed on issues including animal experimentation, agriculture, zoos, and hunting.

Rollin, B.E. (1992). *Animal Rights and Human Morality*. Prometheus Books: Buffalo, N.Y., 248p.

NAL call number: HV4708.R655 1992

Describes theoretical and practical issues related to animals and human morality.

Rollin, B.E. (1995). *Farm Animal Welfare: Social, Bioethical, and Research Issues*. Iowa State University Press: Ames, IO, 168p.

NAL call number: HV4757.R65 1995

Addresses concepts and issues of farm animals welfare and industry methods of animal production.

Rollin, B.E. (1995). *The Frankenstein Syndrome: Ethical and Social Issues in the Genetic Engineering of Animals*. Cambridge University Press: New York, NY, 241p.

NAL call number: QH442.6 R65 1995

A philosophically and scientifically informed discussion of the moral and social issues raised by genetically engineering animals and the real problems society must address to manage the technology.

- Rollin, B.E. (1989). *The Unheeded Cry: Animal Consciousness, Animal Pain and Science*. Oxford University Press: New York, NY, 308p.  
NAL call number: QL55.R65  
Raises questions about the morality of animal use in science and makes recommendations for change. Provides an overview of changing scientific attitudes towards animals.
- Rollin, B.E. and M.L. Kesel (1990). *The Experimental Animal in Biomedical Research*. CRC Press: Boca Raton, FL.  
NAL call number: R853.A53E86 1990  
Vol. 1. A survey of scientific and ethical issues for investigators.
- Rowan, A.N.; F.M. Loew; and J.C. Weer (1994). *The Animal Research Controversy: Protest, Process & Public Policy: An Analysis of Strategic Issues*. Center for Animals & Public Policy, Tufts University School of Veterinary Medicine: North Grafton, MA, 186p.  
NAL call number: HV4708.R68 1994  
This report outlines the current status of animal research, animal numbers, philosophical positions, evaluation of research, alternatives, pain and distress, public debate, education, and suggests policy proposals.
- Sapontzis, S.F. (1987). *Morals, Reason, and Animals*. Temple University Press: Philadelphia, PA, 302p.  
NAL call number: HV4708 S23  
A philosophical look at morals, reason, and man's use of animals. This book argues for animal liberation from human use.
- Shapiro, K.J. (1998). *Animal Models of Human Psychology*. Hogrefe and Huber: Kirkland, WA, 328p.  
An analysis of psychology's use of animals, pros and cons of animal models, and ethical positions.
- Singer, P. (1990). *Animal Liberation*. 2nd edition. Random House: New York, NY, 320p.  
NAL call number: HV4708 S56 1990  
This book defined and defended arguments against human use of animals. The author is a philosopher who is frequently cited during debates on animal rights. A leading proponent of the animal rights movement, the author equates his view of current human attitudes toward animals with racism and sexism. The book includes a history of moral thought regarding animals and their treatment, and cites numerous instances of the use of stressful and painful procedures by researchers.
- Smith, J.A. and K.M. Boyd (1991). *The Ethics of Using Animals in Biomedical Research: The Report of a Working Party of the Institute of Medical Ethics*. Oxford University Press: New York, NY, 352p.  
NAL call number: R853.A53E74 1991
- Tannenbaum, J. (1995). *Veterinary Ethics: Animal Welfare, Client Relations, Competition, and Collegiality*. Mosby: St. Louis, MO, 615p.  
NAL call number: SF756.39 T36 1995

Expression of all views and orientations are provided in the attempt to provide tools that will help veterinary students and practitioners to participate in ethical debates confronting the veterinary profession.

- Webster, J. (1995). *Animal Welfare: A Cool Eye Towards Eden*. Blackwell Science: Cambridge, MA, 273p.  
NAL call number: HV4708 W43 1995  
Describes animal perception and human obligations to pets, wild animals, farm animals, and laboratory animals. Covers mind and suffering, hunger, thirst, and housing.
- Wolfensohn, S. and M. Lloyd (1994). *Handbook of Laboratory Animal Management and Welfare*. Oxford University Press: New York, NY, 304p.  
NAL call number: SF406.W64 1994  
This book is a good introduction to legal, ethical, scientific, and health issues relating to laboratory animal care and use. Contains chapters on pain recognition and alleviation, handling, animal monitoring, surgical techniques, and more.

## **Primates (Nonhuman)**

- Bennett, B.T., R.C. Abee, and R. Henrickson (1995). *Nonhuman Primates in Biomedical Research*. Academic Press: San Diego, CA.  
Part of the American College of Laboratory Animal Medicine series.  
NAL call number: SF407.P7N66 1995  
Covers laws, taxonomy, morphology, behavior, environmental enrichment, conservation, genetics, reproduction, housing, nutrition, record keeping, medical management, breeding, and biosafety.
- Brans, Y.W. and T.J. Kuehl (1988). *Nonhuman Primates in Perinatal Research*. Wiley: New York, NY, 472p.  
NAL call number: RG600.N64 1988  
Sections cover pregnancy, the embryo, fetus, and neonate. Anatomy, physiology, endocrinology, and behavior are described in each section.
- Kirkwood, J.K. and K. Stathatos (1992). *Biology, Rearing, and Care of Young Primates*. Pergamon Press: Oxford; New York, NY, 154p.  
NAL call number: SF408.6.P74K57 1992  
Covers species distribution in the wild, gestation, weaning, energy requirements, growth, and other factors necessary for rearing selected species of nonhuman primates. Species include some prosimians, New World monkeys, Old World monkeys, and gibbons and chimpanzees.
- Jones, T.C., U. Mohr, and R.D. Hunt, eds. (1993). *Nonhuman Primates*. Springer-Verlag: New York, NY, 2 vol.  
NAL call number: RA1199.5.P74N66 1993  
Pathology of nonhuman primates including chapters on immunodeficiency viruses, toxoplasmosis, retroviruses, congenital anomalies, and many others.

- Mench, J.A. and L. Krulisch (1990). *Well-being of Nonhuman Primates in Research*. Scientists Center for Animal Welfare: Greenbelt, MD, 86p.  
NAL call number: QL737.C22C36  
Proceeding from a conference held by the Scientists Center for Animal Welfare. Includes regulatory perspectives, biological perspectives, veterinary perspectives and financial perspectives concerning nonhuman primates.
- National Institutes of Health Office of Animal Care and Use (1991). *National Institutes of Health Nonhuman Primate Management Plan*. National Institutes of Health: Bethesda, MD, 49p.  
NAL call number: HV4758.N3 1991  
The model used for nonhuman primate environmental enrichment programs at the National Institutes of Health. Includes designing, implementing, and evaluating programs as well as species-specific options.
- National Research Council (1998). *The Psychological Well-being of Nonhuman Primates*. National Academy Press: Washington, DC, 168p.  
A review of the literature and suggested guidelines for meeting the psychological needs of primates as specified in the Animal Welfare Act. Covers essentials of programs, general care, special research conditions, prosimians, New and Old World monkeys, apes, and research needs. Also contains samples of nonhuman primate environmental enhancement plans.
- Novak, M.A. and A.J. Petto, eds. (1991). *Through the Looking Glass: Issues of Psychological Wellbeing in Captive Nonhuman Primates*. American Psychological Association: Washington, DC, 285p.  
NAL call number: SF407 P7T49 1991  
Based on a congress held by the American Psychological Association, this book addresses the issues and concerns of nonhuman primate psychological wellbeing.
- Oxnard, C.E., R.H. Crompton, and S.S. Lieverman (1990). *Animal Lifestyles and Anatomies: The Case of the Prosimian Primates*. University of Washington Press: Seattle, WA and London, 174p.  
NAL call number: QL737.P9095.  
A species by species look at prosimian behavior, habitat, and diet in relation to anatomy.
- Segal, E.F. (1989). *Housing, Care and Psychological Well being of Captive and Laboratory Primates*. Noyes Publications: Park Ridge, NJ, 544p.  
NAL call number: QL737.P9H78  
Clearly explores the concepts of environmental enrichment and its connection with proper housing, care, and psychological wellbeing

## Rabbits and Rodents

- Baumans, V., P.F. Brain, H. Brugere, T. Jeneskog, G. Perretta (1994). **Pain and distress in laboratory rodents and lagomorphs: report of the Federation of European Laboratory**



**Animal Science Associations (FELASA) Working Group on pain and distress accepted by the FELASA Board of Management November 1992.** *Laboratory Animals* 28(2):97-112.

NAL call number: QL55.A1L3

Behrend, K. (1991). *Guinea Pigs: Proper Care and Understanding: Expert Advice for Appropriate Maintenance*. Barron's: New York, NY, 63p.

NAL call number: SF459.G9B4413 1991

Geared to the pet owner. Covers housing, husbandry, diet, handling, illness, and breeding.

Dongen, J.J. van, ed. (1990). *Manual of Microsurgery on the Laboratory Rat*. Elsevier: Amsterdam and New York, NY.

NAL call number: RD33.6.M265 1990

Illustrated manual of microsurgical techniques performed on the laboratory rat.

Guttman, H.N. (1990). *Guidelines for the Well-being of Rodents in Research*. Scientists Center for Animal Welfare: Greenbelt, MD, 105p.

NAL call number: HV4704.G8

Proceedings from a 1989 conference. Articles discuss nutrition, cage space, toxicology studies, pain studies, recognition and alleviation of distress and stress, surgery, euthanasia, and mutant mice.

Harkness, J.E. and J.E. Wagner (1995). *The Biology and Medicine of Rabbits and Rodents*. 4th edition. Williams & Wilkins: Baltimore, MD, 372p.

NAL call number: SF996.5.H37 1995

Describes the biology and husbandry of the species, clinical procedures, diagnosis, specific conditions, and case reports.

Hedrich, H.J. and M. Adams (1990). *Genetic Monitoring of Inbred Strains of Rats: A Manual on Colony Management, Basic Monitoring Techniques, and Genetic Variants of the Laboratory Rat*.

Gustav Fischer Verlag: Stuttgart and New York, NY, 539p.

NAL call number: SF407.R38G46

Produced for the International Council for Laboratory Animal Science. Describes colony management, basic monitoring techniques, and genetic variants of the laboratory rat.

Hillyer, E.V. and K.E. Quesenberry (1997). *Ferrets, Rabbits and Rodents: Clinical Medicine and Surgery*. W.B. Saunders: Philadelphia, PA, 432p.

NAL call number: SF997.5.F47F47 1997

Covers ferrets, rabbits, guinea pigs, chinchillas, and small rodents. Sections include diagnosis, surgery, basic anatomy and physiology, radiology, orthopedics, anesthesia, analgesia, and sedation.

Hogan, B. (1994). *Manipulating the Mouse Embryo: A Laboratory Manual*. 2nd edition. Cold Spring Harbor Laboratory Press: Plainview, NY, 497p.

NAL call number: QL737.R6M2468 1994

Provides technical guidance for mouse embryo manipulations and gene therapy.

Institute of Laboratory Animal Resources Committee on Rodents (1996). *Rodents*. National Academy Press: Washington, DC, 167p.  
NAL call number: SF407.R6R62 1996

Hrapkiewicz, K., L. Medina, and D.D. Holmes (1998). *Clinical Laboratory Animal Medicine*. 2nd edition. Iowa State University Press: Ames, IA, 277p.

NAL call number: SF996.5.H65 1998

Species include mice, rats, gerbils, hamsters, guinea pigs, chinchillas, rabbits, ferrets, and nonhuman primates. Each chapter covers housing, husbandry, diseases, surgical and handling techniques, euthanasia, therapeutic agents, and fluid collection. Also includes chapters on serologic testing and quality control, regulations and policies about animal care and use, organizations in laboratory animal medicine, and appendices with normal values.

Institute of Laboratory Animal Resources Committee on Infectious Diseases of Mice and Rats (1991). *Companion Guide to Infectious Diseases of Mice and Rats*. National Academy Press: Washington, DC, 95p.

NAL call number: SF996.5.I54 1991a

Contains sections on disease prevention, specific disease agents, and diagnosis and research complications of infectious agents on the animals and research objectives.

Institute of Laboratory Animal Resources Committee on Infectious Diseases of Mice and Rats (1991). *Infectious Diseases of Mice and Rats*. National Academy Press: Washington, D.C., 397p.

NAL call number: SF996.5.I54 1991

The Committee, under the auspices of the National Research Council, examined rodent disease prevention and individual disease agents and their effects on research. Chapters describe health surveillance programs, barrier programs, diseases of various anatomical systems, and diagnosis and research complications of infectious agents.

Institute of Laboratory Animal Resources Committee on Immunologically Compromised Rodents (1989). *Immunodeficient Rodents: A Guide to Their Immunobiology, Husbandry, and Use*. National Academy Press: Washington, DC, 246p.

NAL call number: RC606.I45

This National Research Council committee gives comprehensive coverage of hereditary immunodeficiencies, induced immunodeficiencies, maintenance of rodents requiring isolation, mating systems for mutants, genetic mechanisms governing resistance or susceptibility to infectious diseases, and hematopoietic cell-surface antigens.

Jackson, R.K. (1997). **Unusual laboratory rodent species: research uses, care, and associated biohazards.** *ILAR Journal* 38(1):13-21.

NAL call number: QL55.A1I43

Covers nontraditional rodents used in biomedical research including marmots, degus, and cotton rats.

Kraft Convener, V., A.A. Deeny, H.M. Blanchet, R. Boot, A.K. Hansen, A. Hem, H. Van Herck, I. Kunstyr, G. Milite, J.R. Needham, W. Nicklas, A. Perrot, C. Reh binder, Y. Richard, and G. De Vroey (1994). **Recommendations for the health monitoring of mouse, rat, hamster, guineapig and rabbit breeding colonies: report of the Federation of European**

**Laboratory Animal Science Associations (FELASA) Working Group on pain and distress accepted by the FELASA Board of Management November 1992.** *Laboratory Animals* 28(1):1-12.

NAL call number: QL55.A1L3

Describes monitoring frequency; sample size; viral, bacterial, mycoplasma, and fungal infections; parasitology; pathology; and necropsy procedures.

Laber-Laird, K., M.M. Swindle, and P.A. Flecknell (1996). *Handbook of Rodent and Rabbit Medicine*. 1st edition. Pergamon: Oxford; Tarrytown, NY, 278p.

NAL call number: SF997.5.R2H36

Covers anesthesia, analgesia, surgical procedures, and drug dosages for rats, mice, gerbils, hamsters, guinea pigs, chinchillas, and rabbits.

Manning, P.J.; D.H. Ringler; and C.E. Newcomer, eds. (1994). *Biology of the Laboratory Rabbit*. 2nd edition. Academic Press: San Diego, CA, 483p.

NAL call number: SF966.5 B56 1994

Describes rabbit anatomy, physiology, housing, husbandry, genetics, and surgical procedures.

Niemi, S.M.; J.S. Venable; and H.N. Guttman, eds. (1994). *Rodents and Rabbits: Current Research Issues*. Scientists Center for Animal Welfare: Greenbelt, MD, 81p.

NAL call number: SF407 R6R63 1994

Proceedings from a 1993 conference. Articles focus on legislation, stress, environmental enrichment, transgenics, anesthesia and analgesia, aseptic surgery, and adjuvant comparisons.

Pass, D. and L. Scott (1993). *Veterinary Care of Birds, Rodents, Rabbits, Ferrets and Guinea Pigs*. Publication no. 93/2. Murdoch University, Foundation for Continuing Veterinary Education: Perth, WA, Australia, 116p.

NAL call number: SF981 V48 1993

Includes management, breeding, biology, anesthesia, reference values, and use of animals in biomedical research.

Suckow, M.A. and F.A. Douglas (1997). *The Laboratory Rabbit*. CRC Press: Boca Raton, FL, 145p.

NAL call number: SF407.R6S83 1997

A volume in *The Laboratory Animal Pocket Reference Series*. Includes sections on biological features, husbandry, management, veterinary care, experimental methodology, and resources. Diagrams show injection, sampling, and catheterization techniques. Drug dosages, antibody production, and safety testing are among the many procedures illustrated.

Van de Weerd, H.A. (1996). *Environmental Enrichment for Laboratory Mice: Preferences and Consequences*. University of Utrecht: The Netherlands, 158p.

Describes strain specific behavioral responses to environmental enrichment, preferences for nesting material and nest boxes, and long term behavioral and physiological effects of enriched and standard housing conditions.

Waynforth, H.B. and P.A. Flecknell (1992). *Experimental and Surgical Technique in the Rat*. Academic Press: London, New York, 382p.

NAL call number: QL737 R666W38 1992



Spiral bound manual with photos and drawings that illustrate administration of substances, methods of obtaining body fluids, anesthesia and postoperative care, surgical technique, specific surgical operations, and miscellaneous techniques such as in vivo perfusions. Vital statistics, drug tradenames and sources, dose rates, identification methods, and other information is provided.

## Surgery

Bojrab, M.J.; S.J. Birchard; and J.L. Tomlinson; eds. (1990). *Current Techniques in Small Animal Surgery*. Lea and Febiger: Philadelphia, PA, 950p.

NAL call number: SF991.C87

An extensive illustrated reference guide to general veterinary surgical techniques and some specific conditions. Contains over 50 chapters covering anatomy, physiology, and surgery of organ systems. Dogs, cats, ferrets, birds, and other small vertebrates are covered.

Bojrab, M.J. and M. Tholen (1990). *Small Animal Oral Medicine and Surgery*. Lea and Febiger: Philadelphia, PA, 270p.

NAL call number: SF992 M68563

Guide to veterinary dental medicine and surgery. Chapters oral and periodontal anatomy, pathology, radiology, extraction techniques and management of associated complications, surgical management of oral neoplasms, periodontal and endodontic therapy, restorative dentistry, orthodontics and dental orthopaedics.

Crow, S.E. and S.O. Walshaw (1997). *Manual of Clinical Procedures in the Dog, Cat, and Rabbit*. 2nd edition. Lippincott-Raven: New York, NY, 323p.

NAL call number: SF991 C76 1997

The purpose of this manual is to provide information on the correct use of diagnostic and therapeutic procedures in veterinary practice. It is a useful tool for veterinary technologists, veterinary students, as well as veterinarians and veterinary technicians in small animal practice or laboratory animal care facilities. The text is organized by procedures, with each described in a step-by-step manner.

Flecknell, P. (1996). *Laboratory Animal Anaesthesia*. 2nd edition. Academic Press: New York, NY, 274p.

NAL call number: SF77.F54 1996

This is a practical guide for researchers and technicians that covers pre- and post-operative care, management of anesthesia, special techniques, and regimens for common laboratory species. Also includes appendices with physiological data, equipment needs, manufacturers and suppliers of drugs, and how to calculate dilutions of anesthetic mixtures.

Gelatt, K.N. and J.P. Gelatt (1994). *Handbook of Small Animal Ophthalmic Surgery*. 1st edition. Pergamon: New York, NY.

NAL call number: SF992.E92G45 1994

Illustrated guide to dog and cat ophthalmic surgery.

Gourley, I.M. and C.R. Gregory (1992). *Atlas of Small Animal Surgery*. Gower Medical Publishing: New York, NY, 161p.



NAL call number: SF991.G68 1992

Small animal surgical techniques including soft tissue techniques are covered in color in this atlas.

Institute of Laboratory Animal Resources Committee on Pain and Distress in Laboratory Animals (1992). *Recognition and Alleviation of Pain and Distress in Laboratory Animals*. National Academy Press: Washington, DC, 137p.

NAL call number: SF996.5.R43 1992

Covers the biology of pain, stress and distress, recognition, control, euthanasia, and recommendations for specific animals.

Kertesz, P. (1993). *Colour Atlas of Veterinary Dentistry & Oral Surgery*. Wolfe Publishing: London, UK, 312p.

This book brings together 720 color photographs, drawings and radiographs relevant to veterinary dentistry and oral surgery in the dog, cat and horse.

Gelatt, K.N. and J.P. Gelatt (1994). *Handbook of Small Animal Ophthalmic Surgery. Volume 1: Extraocular Procedures*. Pergamon Press: Oxford, UK, 195p.

NAL call number: SF992 E92G45 1994

Contains chapters on ophthalmic instrumentation, surgical and operating room equipment, anaesthesia, ophthalmic surgery, and postoperative care. Cats, dogs, birds, and snakes are discussed.

Harvey, C.E., C.D. Newton, and A. Schwartz, eds. (1990). *Small Animal Surgery*. J.B. Lippincott Company: Philadelphia, PA, 670p.

NAL call number: SF911 S52

An illustrated textbook for practitioners and students. Chapters focus on surgical principles, body systems, and organs.

Lumley, J.S.P.; C.J. Green; P. Lear; and J.E. Angell-James (1990). *Essentials of Experimental Surgery*. Butterworth and Co. Ltd.: Boston, MA.

NAL call number: RD29.E8.

Information on the selection and care of laboratory animals, including their housing and husbandry, anaesthesia, tissue surgery, microsurgery, regional surgery, post-operative care and biological measurement techniques.

Noordsy, J.L. (1994). *Food Animal Surgery*. 3rd edition. VLS Books: Trenton, N.J., 302p.

NAL call number: SF911.N65 1994

Describes surgical procedures for swine, cattle, goats, sheep. Useful in animal agriculture and biomedical institutions. Restraint, preoperative and postoperative procedures, anesthesia, and treatment of disease conditions, using fistulas and cannulas, and blood transfusions are discussed.

Orton, E.C., T. McCracken, and J.S. Gaynor (1995). *Small Animal Thoracic Surgery*. Williams & Wilkins: Baltimore, MD, 256p.

NAL call number: SF991.O88 1995

Primarily deals with dog and cat surgery. Includes sections on anesthesia, digestive and cardiopulmonary systems, therapy, instrumentation, techniques, and more.

- Pavletic, M.M. (1993). *Atlas of Small Animal Reconstructive Surgery*. J.B. Lippincott Co.: Philadelphia, PA, 340p.  
NAL call number: SF991.P38 1993  
Describes wound healing, management, and surgery including cosmetic procedures.
- Park, C.M., K.E. Clegg, C.J. Harvey-Clark, and M.J. Hollenberg (1992). **Improved techniques for successful neonatal rat surgery**. *Laboratory Animal Science* 42(5):508-513.  
NAL call number: 410.9 P94  
This article describes surgery in neonatal rats.
- Pratt, P.W., ed. (1985). *Laboratory Procedures for Animal Health Technicians*. American Veterinary Publications, Inc.: Santa Barbara, CA.  
NAL call number: SF772.6.L32.  
Explains the logic behind many laboratory procedures involving animals and describes how they are performed. Covers laboratory tests of blood, urine, organ function, bacteria, and immunity.
- Smith, A.C. and M.M. Swindle, eds. (1994). *Research Animal Anesthesia, Analgesia and Surgery*. Scientists Center for Animal Welfare: Greenbelt, MD, 170p.  
NAL call number: SF914 R49 1994  
Conference proceedings covering pain and distress, anesthesia, analgesia, surgery, post surgical care, laparoscopy, and xenotransplants. Dogs, cats, rodents, rabbits, and farm animals are discussed.
- Tuffery, A.A., ed. (1987). *Laboratory Animals: An Introduction for New Experimenters*. John Wiley & Sons Ltd.: New York, NY, 342p.  
NAL call number: QL55.L274  
A basic reference for many aspects of research animal care and use. Of particular interest are chapters on experimental design, standards of surgery, drug administration, and non-surgical experimental procedures. Other sections include behavior, euthanasia, husbandry, and handling.
- Waynforth, H.B. and P.A. Flecknell (1992). *Experimental and Surgical Technique in the Rat*. Academic Press: London, New York, 382p.  
NAL call number: QL737 R666W38 1992  
Spiral bound manual with photos and drawings that illustrate administration of substances, methods of obtaining body fluids, anesthesia and postoperative care, surgical technique, specific surgical operations, and miscellaneous techniques such as in vivo perfusions. Vital statistics, drug tradenames and sources, dose rates, identification methods, and other information is provided.
- Willard, M.D.; H. Tvedten; G.H. Turnwald (1994). *Small Animal Clinical Diagnosis by Laboratory Methods*. W.B. Saunders Company: Philadelphia, PA, 377p.  
NAL call number: SF991 S59 1994  
Contains chapters on diseases and treatments including reproductive, neurologic, respiratory, and endocrine disorders.

## Wild Animals

- Abbot, S.G. and L.W. Oring (1997). *Guidelines to the Use of Wild Birds in Research*. Special Publication. Ornithological Council: Washington, DC, 52p.  
NAL call number: QL677.5.G75 1997  
Professional guidelines for studies of wild birds in field and laboratory research. Covers permits, investigator impact, collecting and trapping, marking, transport, housing, minor manipulative procedures, and major manipulative procedures including surgery and euthanasia.
- Bayne, K.A.L. and M.D. Kreger, eds. (1995). *Wildlife Mammals as Research Models: In the Laboratory and Field*. Scientists Center for Animal Welfare: Greenbelt, MD, 60p.  
NAL call number: SF406.W55 1995  
Papers from this conference proceedings discuss nonhuman primates in research, other nontraditional mammals, fertility control, methods and ethics of trapping and manipulating wild animals, ethics of maintaining cetaceans in captivity, and use of positive reinforcement to improve animal care and research.
- Dierauf, L.A., ed. (1990). *CRC Handbook of Marine Mammal Medicine: Health, Disease, and Rehabilitation*. CRC Press: Boca Raton, FL, 735p.  
NAL call number: SF997.5.M35C7.  
This book addresses the areas of medicine, surgery, pathology, physiology, feeding and housing, husbandry, stranding and rehabilitation, as well as the natural history of cetaceans, pinnipeds, manatees, sea otters, and polar bears. The book is designed to assist professionals involved in marine mammal health care, wildlife biologists who study these animals in their natural environments, and scientists conducting research on captive and wild marine mammals.
- Driscoll, J.W., ed. (1989). *Animal Care and Use in Behavioral Research: Regulations, Issues, and Applications*. National Agricultural Library, Animal Welfare Information Center: Beltsville, MD, 120p.  
NAL call number: aHv4762 A3A64  
Proceedings of a session at the 1988 meeting of the Animal Behavior Society. The three sections include current regulations in the United States and Canada and methods for complying, general regulatory issues, and methods for improving conditions for captive animals.
- Fowler, M.E. (1995). *Restraint and Handling of Wild and Domestic Animals*. 2nd edition. Iowa State University Press: Ames, IA, 383p.  
NAL call number: QL62.5.F68 1995  
Covers methods of restraint and handling of livestock, laboratory animals, wild animals, and companion animals. Chapters also focus on stress, thermoregulation, and medical problems.
- Fowler, M.E. (1993). *Zoo and Wild Animal Medicine*. 3rd edition. W.B. Saunders: Philadelphia, PA, 617p.  
NAL call number: SF996.Z66-1993  
Includes diseases, pathology, histology, symptoms, and treatment of all animal taxa.

Kleiman, D.G., M.E. Allen, K.V. Thompson, and S. Lumpkin, eds. (1996). *Wild Mammals in Captivity: Principles and Techniques*. University of Chicago Press: Chicago, IL, 639p.

NAL call number: SF408.W55 1996

Contains six parts covering basic husbandry, nutrition, exhibitry, population management, behavior, reproduction, research, and several appendices. Contains information about animal housing, veterinary care, drug dosages, euthanasia, and contraception.

Orlans, F.B. (1988). *Field Research Guidelines: Impact on Animal Care and Use Committees*. Scientists Center for Animal Welfare: Greenbelt, MD, 23p.

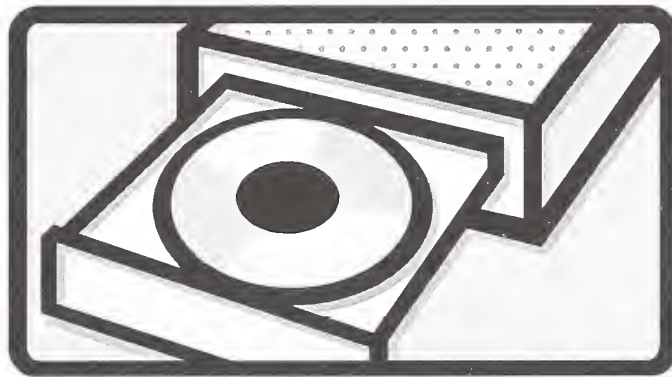
NAL call number: HV4704.F5

The proceedings of a workshop entitled "Field Research Standards" held October 8, 1987.





# Software





## Selected Software Providers

### **Animal Resource Management (ARM)**

8840 Complex Dr., Suite 105, San Diego, CA 92123, phone: (619) 268-4639, fax: (619) 268-1262, e-mail: [arm@tnl-online.com](mailto:arm@tnl-online.com)

Contains modules that automate animal ordering and receiving, tracking, billing, cost accounting, animal care and use protocol design with supporting documents, and drug record maintenance, billing, and inventory.

### **Artac Seel Company**

Post Office Box 296, Basking Ridge, NJ 07920 USA, phone: (973) 425-8997, or 1-888-Just-Asc (U.S. only), fax: (973) 425-0584, e-mail: [JustAsc@ArtacSeel.com](mailto:JustAsc@ArtacSeel.com)  
<http://www.artacseel.com>

TriPhase

Colony, Toxicology and Pathology Data Management

TriPhase, the only single solution for non-clinical research is the combination of products formerly known as Tiger, TecTox and PathData. One vendor with over 180 information specialists, analysts and engineers with a history of solid information systems performance now supports the system customization, interfaces and maintenance. The following modules are available:

ColonyData and GenicData represent the most advanced complete animal facility management software. These modules offer inventory control, ordering cost accounting, animal service breeding systems, identification and license administration. This product has proven to be an efficient tool with high-quality data for logistics and research purposes.

ToxData and ReproData represent a toxicology and repro-toxicology system to support the total preclinical toxicology requirements including study planning, dynamic test article preparation, in-life and clinical pathology, pairing, caesarian section, breeding and skeletal findings.

PathData is an advanced and comprehensive software package designed by pathologists for accurate and highly efficient entry and evaluation of pathology data resulting from toxicology and carcinogenicity studies. Version 4.1C is enhanced with new features and components such as ImageBase, HistoBase and TissueBase.

### **Computer program for reporting health monitoring results in FELASA recommended format**

The Federation of European Laboratory Animal Science Associations (FELASA) has produced recommendations for health screening rodents and rabbits, and defined report formats, see *Laboratory Animals* 30: 193-208.

A Microsoft Excel 5.0 program has been written by Karen Davis, of the Department of Laboratory Animal Science, SmithKline Beecham Pharmaceuticals, to produce health monitoring results in the format recommended for breeding colonies (see *Laboratory Animals* (1994) 28: 1-12) and experimental units (see *Laboratory Animals* 30: 193-208). It enables current results to be entered, these are automatically combined with historical data to produce a standard report incorporating the latest and historical data. Any number of rooms/units can be reported. A copy of the program can be obtained by sending a 3.5 inch disc to: Karen Davis, Department of Laboratory Animal Science,



SmithKline Beecham Pharmaceuticals, Third Avenue, Harlow Essex, CM19 5AD, United Kingdom. Further information from the same address, or by email care of the editor of notes and comments [commentsla@sbphrd.com](mailto:commentsla@sbphrd.com)

### **Topaz Technologies**

13091 Pond Springs Rd., Suite 300, Austin, TX 78729, phone: (512) 249-8080, (800) 274-2273 (U.S. only), fax: (512) 249-8780, e-mail: [topazinfo@topazti.com](mailto:topazinfo@topazti.com)  
<http://www.topazti.com/web/products/products.html>

Produces Granite 4.0 Animal Resources Management Software with four components: facility management, animal records, cost accounting, and training records. The Facility Management System has accounting, animal orders, husbandry, protocol, and system administration components. The protocol component allows processing, creating, and submitting protocols, submission approval, and data management.

### **NTM Consulting Services**

33625 Bardolph Circle, Fremont, CA 94555, phone: (510) 797-3445, fax: (510) 797-0126 e-mail: [Ntmcs@aol.com](mailto:Ntmcs@aol.com) <http://www.ntmcs.com/sirius.htm>

Sirius, NTM's flagship product, is the complete integrated information management tool engineered to reflect the life cycle of animal research: Protocol management, animal procurement, cage card generation, animal and cage census, diagnostic lab & pathology, animal records, personnel training tracking, financials.

Sirius, started in 1994, is the result of a process re-engineering effort by NTM and Stanford University.

### **VETBASE**

Dutch Veterinary Information Systems, Graafschap 7, 3524 TL Utrecht, The Netherlands, fax: +31-30-289-42-51, e-mail: [vetbase@vetinfo.demon.nl](mailto:vetbase@vetinfo.demon.nl)  
<http://www.vetinfo.demon.nl>

VetBase is a searchable veterinary formulary that covers all classes of veterinary drugs except antibiotics. (An updated version containing antibiotics will be available in late 1999.) It currently contains more than 13,000 records of veterinary doses covering more than 800 drugs. Of these, more than 4,500 are for pain management. Animals (more than 170 species!) included in this database include traditional laboratory animals, farm animals, birds, fish, reptiles, amphibians, exotic and zoo animals. VetBase is updated regularly with new information. The database is produced by Hans Kuiper, Ph.D. and Henk-Jan Kuiper, Ph.D. of the Dutch Veterinary Information Systems.

The program is easy to use with its built-in search commands. The user selects an animal and can then search for information based on a pharmaceutical class (anesthetics, analgesics, antiparasitics, etc.), specific drug (ketamine, ivermectin, etc.), or route of administration. The following information is available in the database: drug name, dosage(s), route of administration, notes on use and literature references. The extrapolation routine in the program can be used in cases where there is no dosage listed for a particular species. The routine is based on Kleibers law and extrapolates a specific dose and dosing interval to the dose of another animal type. All in all, it is a handy reference tool that will provide quick answers to drug dosing problems for the busy veterinary professional.

The cost of the program is US \$175 (English version); Hfl 275 (Hfl 323.12 tax included, Dutch version). It will operate on Widows 95 or Windows 98. A Windows NT version is being developed.

The Gerbil Veterinary Formulary 1.1 is a demonstration program of VetBase available free from Dutch Veterinary Information Systems. The *Gerbil Formulary* is an electronic veterinary formulary with 180 dosages for gerbils. The current version contains only non-antibiotic drugs. Download your free copy of *The Gerbil Formulary* today! Go to <http://www.vetinfo.demon.nl>

### **Vetstream**

Vetstream plc, Langford Arch, Sawston, Cambridge CB2 4EG, UK, phone: +44 (0) 1223 500123, fax: +44 (0) 1223 506565, e-mail: [enquiries@vetstream.co.uk](mailto:enquiries@vetstream.co.uk), <http://www.vetstream.com>  
Produces CD-CANIS and CD-Felis, two interactive multimedia CD ROMs that provides clinical information on dog and cat diseases, treatments, symptom descriptions, likely diagnoses, and references. Can be searched by keyword, body system, anatomical area. Training material for veterinarians, graduate students, nursing staff, and others. Workbooks are also available.



# Organizations







## ***North, Central, and South America, and The Caribbean Resources***

### **American Association for Laboratory Animal Science (AALAS)**

9190 Crestwyn Hills Drive  
Memphis, Tennessee 38125, USA

**TELEPHONE:** (901) 754-8620

**FAX:** (901) 753-0046

**E-MAIL:** [info@aalas.org](mailto:info@aalas.org)

**WORLD WIDE WEB:** <http://www.aalas.org>

**CONTACT:** Michael Sondag, Executive Director

**TYPE OF INSTITUTION/ORGANIZATION:** Non-profit, professional

**RESOURCES/SERVICES:** International in scope. Maintains the IACUC Training and Learning Consortium that provides workshops for new and existing IACUC members. Serves as a clearinghouse for collection and exchange of information on all phases of laboratory animal care and management, use and procurement of laboratory animals used in biomedical research. Educational materials, guides, and audiovisuals. Holds annual meetings. Publishes *Contemporary Topics* - a bimonthly journal with an expanded peer reviewed section on topics such as clinical management and husbandry. Also publish *Laboratory Animal* - a monthly, peer reviewed journal covering a diverse array of applied and experimental topics in the laboratory animal sciences.

**REQUESTOR:** Anyone.

**COSTS:** Charge for materials (members are charged a lower rate).

### **American College of Laboratory Animal Medicine**

96 Chester Street  
Chester, NH 03036 USA

**TELEPHONE:** (603) 887-2467

**FAX:** (603) 887-0096

**E-MAIL:** [mwbaclam@gsinet.net](mailto:mwbaclam@gsinet.net)

**WORLD WIDE WEB:** <http://www.aclam.org>

**CONTACT:** Dr. Melvin W. Balk, Executive Director

**TYPE OF INSTITUTION/ORGANIZATION:** Non-profit, professional

**RESOURCES/SERVICES:** The American College of Laboratory Animal Medicine (ACLAM) is an organization of board certified veterinary medical specialists who are experts in the humane, proper and safe care and use of laboratory animals. ACLAM establishes standards of education, training, experience and expertise necessary to become qualified as a specialist and recognizes that achievement through board certification. ACLAM actively promotes the advancement of knowledge in this field through professional continuing education activities, the development of educational materials and the conduct of research in laboratory animal medicine and science.

**REQUESTOR:** Veterinarians and laboratory animal users.

**COSTS:** Charge for materials, see website.

## **American Society of Laboratory Animal Practitioners**

c/o Bradford S. Goodwin, Jr., DVM  
Secretary - Treasurer  
University of Texas Medical School  
6431 Fannin, Room 1.132  
Houston, TX 77030-1501

**TELEPHONE:** (713) 500-7542

**FAX:** (713) 500-0534

**E-MAIL:** [bgoodwin@admin4.hsc.uth.tmc.edu](mailto:bgoodwin@admin4.hsc.uth.tmc.edu)

**WORLD WIDE WEB:** <http://www.aslap.org>

**CONTACT:** Bradford S. Goodwin, Jr., DVM, Secretary - Treasurer

**TYPE OF INSTITUTION/ORGANIZATION:** Nonprofit, professional society.

**RESOURCES/SERVICES:** ASLAP provides the following: (1) EDUCATIONAL SESSIONS: Dealing with practical problems, sessions are held during annual AVMA and AALAS meetings. Continuing education seminars are held every two years; (2) ASLAP NEWSLETTER: The official publication of ASLAP, is circulated quarterly to the membership and veterinary school libraries; and (3) DIRECTORY: Hand in hand with continuing education, the Society recognizes the importance of cooperation among members in the distribution of information. A list of members and their areas of interest is maintained and distributed to the membership. In addition, AVMA members are eligible for the **ASLAP Excellence in Laboratory Animal Research Award**.

**REQUESTOR:** Laboratory animal veterinarians.

**COSTS:** Dues are \$45.00 if paid on or before March 31st of each year and \$55.00 if paid on or after April 1st of each year. Student membership dues are \$22.50 before April 1st and \$27.50 after.

## **Animal Care**

United States Department of Agriculture  
Animal and Plant Health Inspection Service  
4700 River Road, Suite 6D02  
Riverdale, Maryland 20734-1234, USA

**TELEPHONE:** (301) 734-4980

**FAX:** (301) 734-4328

**E-MAIL:** [ace@aphis.usda.gov](mailto:ace@aphis.usda.gov)

**WORLD WIDE WEB:** <http://www.aphis.usda.gov/ac>

**CONTACT:** Deputy Administrator

**TYPE OF INSTITUTION/ORGANIZATION:** Federal government

**RESOURCES/SERVICES:** Federal regulatory agency with oversight of the Animal Welfare Act and animal welfare regulations. Routinely inspects regulated facilities and provides guidance on animal welfare compliance issues. Can provide copies of the USDA animal welfare regulations. Web site provides access to electronic Freedom of Information Act (FOIA) documents, full-text versions of the Animal Welfare Act, animal welfare regulations, Animal Care policies, IACUC checklists, Horse Protection Act information, and other information pertaining to the use of animals in nonagricultural commerce.

**REQUESTOR:** Anyone.

**COSTS:** free.

## **Animal Welfare Information Center (AWIC)**

United States Department of Agriculture  
Agricultural Research Service  
National Agricultural Library  
10301 Baltimore Avenue  
Beltsville, Maryland 20705, USA

**TELEPHONE:** (301) 504-6212

**FAX:** (301) 504-7125

**E-MAIL:** [awic@nal.usda.gov](mailto:awic@nal.usda.gov)

**WORLD WIDE WEB:** <http://www.nal.usda.gov/awic>

**CONTACT:** Jean Larson, Coordinator

**TYPE OF INSTITUTION/ORGANIZATION:** Federal government

**RESOURCES/SERVICES:** Vast collection of serials, monographs, and audiovisuals within the National Agricultural Library (NAL). Documents may be borrowed through an interlibrary loan. For more information on document delivery, contact (301) 504-5755. The Center performs brief complimentary searches of AGRICOLA and other relevant databases. The Center can also assist you in formulating your own database searches, provides conference facilities and host training sessions, and can make available speakers and/or a tabletop exhibit for training sessions, conferences, and workshops. The Center produces bibliographies on topics such as stress, analgesia, animal testing alternatives, training materials and other relevant topics to animal welfare. Publishes the *Animal Welfare Information Center Bulletin*.

**REQUESTOR:** Anyone.

**COSTS:** All publications are available for free; literature searches on a cost recovery basis; NAL may charge for certain services such as providing photocopies, document delivery, etc.

## **Animales de Experimentación**

La Revista Hispanoamericana  
AP27-281 México, D.F. 06761 MEXICO

**TELEPHONE:** (525) 264-3887

**FAX:** (525) 574-3225

**E-MAIL:** [ciro@servidor.unam.mx](mailto:ciro@servidor.unam.mx)

**CONTACT:** Dr. Ciro Lomelí, Editor and Director

**TYPE OF INSTITUTION/ORGANIZATION:** Organization journal.

**RESOURCES/SERVICES:** The official journal of the Central America, Caribbean and Mexican Association For Laboratory Animal Science (ACCMAL) and the Mexican Association for Laboratory Animal Science (AMCAL,A.C.). A Spanish language journal that is distributed in the United States, Spain, and 20 Latin American countries. The mission is to disseminate scientific and technological advances related to animal production, responsible care and use of animals in scientific experiments, testing, and education. It also serves as a communication venue among Spanish-speaking individuals interested in biomedicine and laboratory animal medicine and science.

**REQUESTOR:** Anyone.

**COSTS:** Annual subscription is: Mexico-350 Pesos; U.S. and other countries US\$40.



**Applied Research Ethics National Association  
(ARENA)**

132 Boylston Street, Fourth Floor  
Boston, Massachusetts 02116, USA

**TELEPHONE:** (617) 423-4112

**FAX:** (617) 423-1185

**EMAIL:** [PRMR@aol.com](mailto:PRMR@aol.com)

**WORLD WIDE WEB:** <http://www.anes.hmc.psu.edu/ArenaFolder/ArenaHome.html>

**TYPE OF INSTITUTION/ORGANIZATION:** Non-profit

**RESOURCES/SERVICES:** A membership organization for those involved in the day-to-day application of ethical principles, governmental regulations, and other policies regarding research and clinical practice. ARENA's services include: (1) the sponsorship of national and regional meetings to review and shape research policy; (2) the dissemination of current information on research ethics issues, and the provision of opportunities for networking among members through a quarterly newsletter; (3) the distribution of the Animal Care and Use Committee Guidebook, which was published by ARENA/OPRR in cooperation with the National Institutes of Health; (4) assistance with the development of regional networks; (5) providing access to consultants expert in specific bioethical issues and administrative operations; (6) the publication of an annual comprehensive directory of ARENA members; (7) the preparation of commentary on and responses to relevant federal legislative or administrative initiatives; and (8) the ARENA Mailing List which is an electronic mailing list for members of the Applied Research Ethics National Association (ARENA). This is a closed list, available to members of ARENA only. Its purpose is to provide a forum for ARENA members to communicate with each other on matters related to the concerns of institutional review boards (IRBs) and institutional animal care and use committees (IACUCs).

**REQUESTOR:** Anyone but some activities are restricted to members.

**COSTS:** Varies.

**Association For Assessment and Accreditation of Laboratory Animal Care  
International (AAALAC International)**

11300 Rockville Pike, Suite 1211

Rockville, Maryland 20852-3035 USA

Avenue de Tervueren 402

1150 Brussels, BELGIUM

**TELEPHONE:** (301) 231-5353

**FAX:** (301) 231-8282

**E-Mail:** [accredit@aaalac.org](mailto:accredit@aaalac.org)

**WORLD WIDE WEB:** [www.aaalac.org](http://www.aaalac.org)

**CONTACT:** John Miller, D.V.M.

32 2 761 66 78

32 2 761 66 79

[accredit\\_europe@aaalac.org](mailto:accredit_europe@aaalac.org)

**TYPE OF INSTITUTION /ORGANIZATION:** Non-profit, professional

**RESOURCES/SERVICES:** Like other animal welfare organizations, AAALAC International, the Association for Assessment and Accreditation of Laboratory Animal Care, supports the use of animals to advance medicine and science when there are no non-animal alternatives, and when it is done in an ethical and humane way. When animals are used, AAALAC works with institutions and researchers to serve as a bridge between progress and animal well-being. This is done through a voluntary accreditation program in which research institutions demonstrate that they are not only meeting the minimums required by law, but are going the extra step to achieve and showcase

excellence in animal care and use. Separate from accreditation, AAALAC also offers independent assessments of animal research programs to help institutions continue to improve their animal care and use practices.

**REQUESTORS:** Laboratory animal professionals.

**COSTS:** Vary according to services.

### **Canadian Association for Laboratory Animal Science**

#### **L'Association Canadienne Pour La Technologies des Animaux de Laboratoire**

c/o CALAS/ACSAL National Office

PO Box 34122 RPO Fort Richmond

Winnipeg, Manitoba R3T 5T5

**TELEPHONE:** (204) 261-7534

**FAX:** (204) 261-7619

**E-MAIL:** [webmaster@calas-acsal.org](mailto:webmaster@calas-acsal.org)

**WWW:** <http://www.calas-acsal.org/>

**CONTACT:** Bob Madziak

**TYPE OF INSTITUTION/ORGANIZATION:** Professional, nonprofit

**RESOURCES/SERVICES:** Produces educational materials, training videos, and a monthly newsletter (CALAS/ACSAL Newsletter). Hold annual meetings with workshops, seminars, and poster sessions.

**REQUESTOR:** Laboratory animal professionals.

**COSTS:** Vary according to materials.

### **Canadian Council on Animal Care (CCAC)**

350 Albert Street, Suite 315

Ottawa, Ontario K1R 1B1, CANADA

**TELEPHONE:** (613) 238-4031

**FAX:** (613) 238-2837

**E-MAIL:** [ggriffin@bart.ccac.ca](mailto:ggriffin@bart.ccac.ca)

**WORLD WIDE WEB:** [www.ccac.ca](http://www.ccac.ca)

**CONTACT:** Dr. James Wong, Director of Assessments

**TYPE OF INSTITUTION/ORGANIZATION:** Private, non-profit

**RESOURCES/SERVICES:** Establishment and enforcement of standards and guidelines (in Canada) concerning the use of animals in research, testing and teaching. Maintains active, expert committees on all aspects of animal care and use. The Council's program is based on its major publication *Guide to the Care and Use of Experimental Animals*, Volume 1, 2nd Edition (1993) and Volume 2 (1984). More recent guidelines (available through their website are: *animal use protocol review*, *transgenic animals*, and *choosing an appropriate endpoint in experiments using animals for research, teaching, and testing*. CCAC conducts workshops and training courses on various aspects of the care and use of experimental animals, as well as the training of personnel working with these animals. The Council addresses alternative methods and conducts a course on tissue culture. Semi-annually publishes the newsletter, *Resource*.

**REQUESTOR:** Anyone.

**COSTS:** Vary according to materials.

## **Institute of Laboratory Animal Resources (ILAR)**

National Academy of Sciences  
2101 Constitution Avenue, N.W.

Washington, D.C. (District of Columbia) 20418, USA

**TELEPHONE:** (202) 334-2590

**FAX:** (202) 334-1687

**E-MAIL:** [ILAR@nas.edu](mailto:ILAR@nas.edu)

**WORLD WIDE WEB:** <http://www4.nas.edu/cls/ilarhome.nsf>

**CONTACT:** Ralph Dell

**TYPE OF INSTITUTION/ORGANIZATION:** ILAR is a unit of the National Research Council's (NRC) Commission on Life Sciences (CLS). The NRC is the working arm of the National Academy of Sciences (NAS), a private, non-governmental, non-profit organization.

**RESOURCES/SERVICES:** Information on a wide variety of topics related to laboratory animals and emerging adjuncts and alternatives to animal use. Assignments of genetic identification for unique colonies. Guidelines that assist in the implementation of national policies or laws. Information to teachers and students about animals in science and careers in biology. ILAR's information database, which is published as *Animals for Research: A Directory of Sources*. This assists scientists in locating specific animals and models, including nonhuman primates. Produces *ILAR Journal* - a quarterly journal, available free-of-charge to institutional animal care and use committees, scientists, and veterinarians. Reports specific to nonhuman primates such as *Laboratory Animal Management: Nonhuman Primates*. Manages *Animal Models and Genetic Stocks Information Exchange Program*.

**REQUESTOR:** Anyone.

**COSTS:** Vary according to materials.

## **Laboratory Animal Management Association (LAMA)**

P.O.Box 877

Killingworth, Connecticut 06419, USA

**TELEPHONE:** (301) 295-1568

**FAX:** (301) 295-0947

**E-MAIL:** [Weichbrod@vax.afri.usuhs.mil](mailto:Weichbrod@vax.afri.usuhs.mil)

**WORLD WIDE WEB:** <http://www.animalvillage.com/lama/>

**CONTACT:** Robert Weichbrod, Editor, LAMA Review

**TYPE OF INSTITUTION/ORGANIZATION:** Professional

**RESOURCES/SERVICES:** LAMA was organized in 1984 to promote the dissemination of ideas, experience, and knowledge, to encourage continued education, and to assist in the training of laboratory animal facility managers. It accomplishes this through: The LAMA Review - a quarterly publication dedicated to providing laboratory animal management information; LAMA Lines - a newsletter published six times a year informing the membership of what is going on in the organization; LAMA Membership Directory - an information resource for those in supervision through "networking" with others dealing with similar issues (member phone numbers, fax, and email addresses); LAMA Mid-year Forum - a day and a half event, seminar, workshop and tour of facilities or manufacturing plants; Annual Educational Program - a full day combination event, seminar, workshop and tour of facilities or manufacturing plants,

**REQUESTORS:** Members.

**COSTS:** \$30.00 per year (US currency).



## **Laboratory Animal Welfare Training Exchange**

Washington University School of Medicine

Division of Comparative Medicine

660 S. Euclid Avenue

St. Louis, Missouri 63110, USA

**TELEPHONE:** (314) 362-4516

**FAX:** (314) 362-6480

**E-MAIL:** [nicole@dcm.wustl.edu](mailto:nicole@dcm.wustl.edu)

**WORLD WIDE WEB:** <http://www.lawte.org>

**CONTACT:** Nicole Duffee, D.V.M., Ph.D., President

**TYPE OF INSTITUTION/ORGANIZATION:** non-profit

**RESOURCES/SERVICES:** Holds conferences every two years for trainers to exchange information on their training programs. Past years conference proceedings are available on the LAWTE web site. Audio and video tapes are also available of conference presentations. Also maintains the LAWTE listserv for networking among trainers and training coordinators on issues and methods of training in the laboratory animal field.

**REQUESTORS:** Anyone; members receive other benefits.

**COSTS:** Membership dues are \$10 annually; audiotapes are \$12, videotapes are \$15.

## **Latin American Society of Animal Welfare**

Universidad del Salvador

Campus Nuestra Sra. del Pilar

1629 C.C. 198

Pilar, Provincia de Buenos Aires

ARGENTINA

**TELEPHONE:** +54 2 322 4 31260

**FAX:** +54 2 322 4 31263

**E-MAIL:** [uds-vete@salvador.edu.ar](mailto:uds-vete@salvador.edu.ar)

**WORLD WIDE WEB:** <http://www.salvador.edu.ar/uaf3-2.htm>

**CONTACT:** Leopoldo Estol, D.V.M.

**TYPE OF INSTITUTION/RESOURCE:** Professional

**RESOURCES:** This organization was established in October 1998 to promote the teaching of animal welfare, bioethics, and ethology in university curricula.

## **National Library of Medicine (NLM)**

8600 Rockville Pike

Bethesda, Maryland 20894, USA

**TELEPHONE:** (301) 496-6095 or 1-800-272-4787

**FAX:** (301) 402-1384

**E-MAIL:** [ref@nlm.nih.gov](mailto:ref@nlm.nih.gov)

**WORLD WIDE WEB:** <http://www.nlm.nih.gov/>

**TYPE OF INSTITUTION/ORGANIZATION:** Federal government

**RESOURCES/SERVICES:** Library - extensive collection of serials, monographs, audiovisuals can be accessed by anyone. Computer based systems of information retrieval include MEDLARS, MEDLINE, CANCERLIT, AVLINE, TOXLINE, and Grateful Med.



**REQUESTOR:** Anyone.

**COSTS:** \$7.00 for each filled interlibrary loan.

### **Office for Protection from Research Risks**

Division of Animal Welfare  
National Institutes of Health  
6100 Executive Boulevard, Suite 3B01  
Rockville, Maryland 20892-7507, USA

**TELEPHONE:** (301) 496-7163

**FAX:** (301) 402-2803

**E-MAIL:** [oprr@od.nih.gov](mailto:oprr@od.nih.gov)

**WORLD WIDE WEB:** <http://grants.nih.gov/grants/oprr/oprr.htm#LAB>

**CONTACT:** Division of Animal Welfare

**TYPE OF INSTITUTION/ORGANIZATION:** Federal government

**RESOURCES/SERVICES:** (1) Directs the development, implementation, and compliance oversight activities for the PHS Policy on Humane Care and Use of Laboratory Animals; (2) exercises oversight and negotiates Assurances of Compliance in all areas of laboratory animal research; (3) maintains liaison and coordinates policy implementation with components throughout PHS that conduct or support research involving laboratory animals; and (4) directs the development and implementation of educational and instructional programs and generates resource materials relating to the responsibilities of the research community for the appropriate care and use of laboratory animals. Provides regional workshops for IACUCs and scientists on various topics related to laboratory animals. Can provide guidance to IACUCs on issues involving the use of animals in research and compliance with Public Health Service policy and guidelines. On its website you can find: (1) an interactive tutorial for new animal care and use committee members, institutional administrators, investigators, animal care personnel, veterinarians, or others interested in learning about the PHS Policy on Humane Care and Use of Laboratory Animals; (2) sample annual reports, animal welfare assurances, semiannual review checklist, and semiannual report to the institutional official, to aid institutions in implementing the PHS Policy; and (3) the PHS Policy on Humane Care and Use of Laboratory Animals, policy guidance, articles, OPRR Reports, IACUC Guidebook, and other materials relevant to laboratory animal welfare).

**REQUESTOR:** Anyone.

**COST:** Most materials are free of charge except for national animal welfare workshops.

### **Public Responsibility in Medicine and Research (PRIM & R)**

Fourth Floor  
132 Boylston Street  
Boston, Massachusetts 02116, USA

**TELEPHONE:** (617) 423-4112

**FAX:** (617) 423-1185

**E-MAIL:** [PRMR@aol.com](mailto:PRMR@aol.com)

**WORLD WIDE WEB:** <http://www.aamc.org/research/primr/descriptn.htm>

**CONTACT:** Joan Rachlin, Executive Director

**TYPE OF INSTITUTION/ORGANIZATION:** Non-profit

**RESOURCES/SERVICES:** Through PRIM&R conferences, a wide range of issues regarding research using animals and the operation of IACUC's have been discussed. Extensive workshop manuals are provided to conference attendees. The annual IACUC conference also plays host to IACUC 101, a primer for new IACUC members and those wishing additional training in the workings of these committees.

**REQUESTORS:** Anyone

**COSTS:** Conference proceedings are \$30; fees for annual conferences vary.

### **Scientists Center for Animal Welfare (SCAW)**

Golden Triangle Building One  
7833 Walker Drive, Suite 340  
Greenbelt, Maryland 20770, USA

**TELEPHONE:** (301) 345-3500

**FAX:** (301) 345-3503

**E-MAIL:** [info@scaw.com](mailto:info@scaw.com)

**WORLD WIDE WEB:** <http://www.scaw.com>

**CONTACT:** Lee Krulisch, Executive Director

**TYPE OF INSTITUTION/ORGANIZATION:** Private, non-profit

**RESOURCES/SERVICES:** Publications, including conference proceedings, training manuals, and materials from other organizations. Publications - extensive listing of publications of direct relevance to IACUC activities. Each contains proceedings from conferences sponsored by SCAW. Maintains IACUC-Talk- a moderated listserv for discussion of IACUC issues.

**REQUESTOR:** Anyone.

**COSTS:** Some services are free, meeting registration fees vary. Regular Membership \$40, Student Membership \$15, Foreign Membership \$60.

## ***European, Asian, and Australian Resources***

### **Australian and New Zealand Council for the Care of Animals in Research and Teaching, Limited (ANZCCART)**

P.O. Box 19  
Glen Osmond SA 5064  
AUSTRALIA

P.O. Box 598  
5064 Wellington  
NEW ZEALAND

**TELEPHONE:** 61-83-03-73-93 (Australia)

**FAX:** 61-83-79-38-80 (Australia)

**E-MAIL:** Australia- [anzccart@waite.adelaide.edu.au](mailto:anzccart@waite.adelaide.edu.au)

New Zealand- [anzccart@rsnz.govt.nz](mailto:anzccart@rsnz.govt.nz)

**WORLD WIDE WEB:** Australia <http://www.adelaide.edu.au>

New Zealand <http://anzccart.rsnz.govt.nz>

**CONTACT:** R.M. Baker

**TYPE OF INSTITUTION/ORGANIZATION:** private, non-profit

**RESOURCES/SERVICES:** Quarterly newsletter, and other publications on euthanasia, animal care and use committees, well-being of research animals, alternatives for undergraduate education, laboratory animal surveys, tumor cell lines available in Australia, humane care and use of animals in research, and animal pain.

**REQUESTOR:** Anyone.

**COSTS:** Vary according to materials.

### **Baltic Laboratory Animal Science Association**

53 Krustpils Street  
Riga, LV-1057 LATVIA

**TELEPHONE:** +371 7139461

**FAX:** +371 7139513

**E-MAIL:** [bjlanim@grindeks.lv](mailto:bjlanim@grindeks.lv)

**WWW:** <http://vip.latnet.lv/journalLAS/> (Journal homepage)

**CONTACT:** Guna Jacobson, Executive Director

**TYPE OF INSTITUTION/ORGANIZATION:** Non-profit, professional society

**RESOURCES/SERVICES:** Publishes a quarterly journal (Baltic Journal of Laboratory Animal Science—see web address above), sponsors training courses for scientists and technicians based on FELASA recommendations, and co-sponsors annual meetings with other European laboratory animal science associations.

**REQUESTOR:** Anyone.

**COSTS:** The journal subscription price including postage for 1999 for one volume (4 issues) is US\$90 for European countries and US\$100 for others. Certain discount is given to subscribers from Baltic and former USSR states. Prices for courses and conferences varies.

## **European Biomedical Research Association**

58 Great Marlborough Street  
London W1V 1DD UNITED KINGDOM

**E-MAIL:** [secretariat@ebra.org](mailto:secretariat@ebra.org)

**WORLD WIDE WEB:** <http://www.ebra.org>

**CONTACT:** Dr. Mark Matfield, Secretariat Director

**TYPE OF INSTITUTION/ORGANIZATION:** non-profit

**RESOURCES/SERVICES:** EBRA is an association of individuals and organisations in the scientific, medical and veterinary professions in the countries of the Council of Europe. EBRA was established to promote the public understanding of the importance of animals in medical and veterinary research and safety testing. The main activities of EBRA are: (1) Producing and distributing a European bulletin about the use of animals in medical research and testing, the activities of campaigning groups and relevant legislative matters in individual countries and throughout the European Union; (2) Assisting individual and corporate members across Europe to promote a balanced and accurate representation of animal research in their national press; (3) Ensuring that accurate and relevant information about animal research is available to European politicians and officials; (4) Ensuring that the views of animal researchers are properly represented to European politicians and officials; (5) Ensuring that information about best practice in laboratory animal science and welfare is readily available within the European scientific community and applied throughout Europe; (6) Maintaining an e-mail bulletin service for members of EBRA. The website provides information on European statistics on animal research, regulation of animal research in European countries, and European research news.

**REQUESTORS:** Anyone

**COSTS:** The annual subscription for Individual Membership is currently ECU 15 per annum.

## **European Society of Laboratory Animal Veterinarians**

c/o Philippe J. R. Baneux, DVM  
Pfizer Research Center  
BP 159  
F-37401 Amboise FRANCE

**E-MAIL:** [Philippe.Baneux@pfizer.com](mailto:Philippe.Baneux@pfizer.com) or [pnowlan@tcd.ie](mailto:pnowlan@tcd.ie)

**WORLD WIDE WEB:** <http://www.eslav.org>

**CONTACT:** Philippe Baneux, President

**TYPE OF INSTITUTION/RESOURCE:** non-profit

**RESOURCES/SERVICES:** One of the objectives of the Society is to give veterinarians a forum to discuss issues which concern us, in the field of laboratory animal science, in general and in Europe specifically. Veterinarians who work full time or part time, as consultants in this field need to keep themselves updated with regards to e.g. changing and evolving laws and regulations in Europe and in individual nations as well as world wide. Another important objective of this Society is to set the right environment and support to create the European College of Laboratory Animal Medicine. This College is needed to structure the additional training leading to specialization and to certify its members, and to provide assistance in ESLAV's professional continuing education activities. In other words, the College will represent the academic component in our field of laboratory animal medicine. The objectives of ESLAV shall be achieved through: Meetings, lectures, discussions, and publications. These objectives are: (1) The advancement of veterinary knowledge and skills in



subjects connected with the breeding, health, welfare, and use of laboratory animals; (2) Collaboration and exchange of information with other societies and allied scientific disciplines (3) Actively encouraging its members to provide training for veterinarians practicing or wishing to practice in the field of laboratory animals, both at the under and post graduate level. Holds meetings jointly with FELASA and other organizations.

**REQUESTORS:** Laboratory animal veterinarians

**COSTS:** Annual membership fees have been set at 250 French Francs.

## **Federation of European Laboratory Animal Science Associations (FELASA)**

BCM Box 2989

London WC1N 3XX, UNITED KINGDOM

**CONTACT:** P. Hardy, Secretary

**WORLD WIDE WEB:** <http://www.felasa.org> (under construction)

**TYPE OF INSTITUTION/ORGANIZATION:** Professional

**RESOURCES/SERVICES:** Co-sponsor of *Laboratory Animals: The International Journal of Laboratory Animal Science and Welfare*. Sponsors annual animal welfare symposiums.

**REQUESTOR:** Laboratory animal users.

**COSTS:** Vary according to materials.

## **Fund for the Replacement of Animals in Medical Experiments (FRAME)**

Russell & Burch House,

96-98 North Sherwood Street,

Nottingham NG1 4EE UNITED KINGDOM

**TELEPHONE:** +44 (0)115 958 4740

**FAX:** +44 (0)115 950 3570

**E-MAIL:** [frame@frame-uk.demon.co.uk](mailto:frame@frame-uk.demon.co.uk)

**WORLD WIDE WEB:** <http://www.frame-uk.demon.co.uk/>

**CONTACT:** Professor Robert Combes, Scientific Director

**TYPE OF INSTITUTION/RESOURCE:** non-profit

**RESOURCES/SERVICES:** FRAME publishes a scientific journal, *ATLA (Alternatives To Laboratory Animals)* that appears six times a year and contains original scientific papers, reports of ECVAM (European Centre for the Validation of Alternative Methods) workshops, comments and news and views articles. FRAME also publishes an influential newsletter, *FRAME News*, aimed at scientists, politicians, administrators and the informed general public. Subscription is 15 UK pounds (30 US dollars) per year. *Friends of FRAME* is published for FRAME individual supporters. *Selection and use of replacement methods in animal experimentation*, a 32-page booklet produced by FRAME and UFAW, gives a brief overview of alternatives to the use of animals, together with indications of where to find more-detailed information. A copy of the booklet has been sent to all centers licensed for animal experimentation in Britain. Copies are available for purchase from UFAW. FRAME also teaches workshops on The Information Requirements of the Animals (Scientific Procedures) Act, to assist researchers in performing literature searches for alternatives.

**REQUESTORS:** Anyone.

**COSTS:** Varies according to materials. Individuals who support the aims of FRAME may join *Friends of FRAME* at an annual subscription of 15 UK pounds. Members receive *FRAME News* and the *Friends of FRAME* newsletter.

**Gesellschaft für Versuchstierkunde  
Society for Laboratory Animal Science (GV-SOLAS)**

Zentrale Tierlaboratorien  
Freie Universität Berlin  
Kraemerstrasse 6  
D-12207 Berlin  
GERMANY

**TELEPHONE:** +49 30 / 8445 38 33

**FAX:** +49 30 / 833 93 89

**E-MAIL:** [treiber@uni-duesseldorf.de](mailto:treiber@uni-duesseldorf.de) (will contact Dr. Annemarie Treiber, GV-SOLAS President)

**WORLD WIDE WEB:** <http://www.mh-hannover.de/institut/tierlabor/gv-solas/>

**CONTACT:** Dr. Hans Hiller, Secretary (via phone or fax only)

**TYPE OF INSTITUTION/ORGANIZATION:** Professional

**RESOURCES/SERVICES:** Co-sponsor of *Laboratory Animals: The International Journal of Laboratory Animal Science and Welfare*. Also sponsors conferences and makes other publications available.

**REQUESTOR:** Laboratory animal users.

**COSTS:** Vary according to materials.

**Institute of Animal Technology**

C/o Registered Offices  
5 South Parade  
Summertown

Oxford OX2 7JL UNITED KINGDOM

**E-MAIL:** [Chairman@iat.org.uk](mailto:Chairman@iat.org.uk)

**WORLD WIDE WEB:** <http://www.iat.org.uk/>

**CONTACT:** Chairman

**TYPE OF INSTITUTION/ORGANIZATION:** Nonprofit, professional society.

**RESOURCES/SERVICES:** Publishes the journal *Animal Technology* and the monthly *Bulletin of the Institute of Animal Technology*. *Bulletins* carry the latest news and views on development in animal technology, branch events and employment vacancies. Produces or makes available videos and training manuals on humane care and handling. The IAT provides an opportunity to promote products and services through its publications, congress, symposia and also through sponsorship.

**REQUESTOR:** Laboratory animal users.

**COSTS:** Vary according to material; membership fees vary according to level.

**Institut für Labortierkunde der Universität Zürich  
Institute of Laboratory Animal Science**

University of Zurich  
Winterthurerstrasse 190  
8057 Zurich, SWITZERLAND

**TELEPHONE:** + 41 1 / 635 11 11 or + 41 1 / 635 54 51

**FAX:** +41 1 / 635 57 03

**E-MAIL:** [ptho@ltk.unizh.ch](mailto:ptho@ltk.unizh.ch)

**CONTACT:** Prof. Dr. med. vet. Peter E. Thomann, Director

**WORLD WIDE WEB:** <http://www.unizh.ch/labtier/>

**TYPE OF INSTITUTION/ORGANIZATION:** University

**RESOURCES/SERVICES:** Provides classes and training courses for technicians, students and postgraduates. Breeds rats and mice, offers diagnostic services for rodents and rabbits, offers in vitro production of monoclonal antibodies, and operates a consulting service to answer questions relating to the care of laboratory animals. Most information on the Web site is in German.

**REQUESTOR:** Laboratory animal users.

**COSTS:** Vary according to material.

### **Japanese Association for Laboratory Animal Science (JALAS)**

2-8-10 Iwamotocho

Chiyoda-ku

Tokyo 101, JAPAN

**TELEPHONE/ FAX:** 03-3865-1475

**RESOURCES:** Publishes the quarterly journal *Experimental Animals*.

**COSTS:** Price of one issue is 2,500 yen (US \$25) for non-member individual.

### **Laboratory Animal Science Association (LASA)**

P.O. Box 3993

Tamworth, Staffs B78 3QU, UNITED KINGDOM

**TELEPHONE:** 01827 260036

**FAX:** 01827 260036

**E-MAIL:** [lasa@globalnet.co.uk](mailto:lasa@globalnet.co.uk)

**WORLD WIDE WEB:** <http://www.mandm.ncl.ac.uk/lasa.html>

**CONTACT:** B.R. Howard, Honorary Secretary

**RESOURCES/SERVICES:** Co-sponsor of *Laboratory Animals: The International Journal of Laboratory Animal Science and Welfare*. Other services include: (1) The opportunity to network with other experts in the field and exchange views and information; (2) Career development through education and training; (3) Strong, influential representation of your opinions and concerns at national and international level; (4) Regular quarterly newsletter with topical news, comment and feature articles about LASA's activities and the world of laboratory animal science (5) Key issues reported in-depth through "Laboratory Animals" - the official journal of LASA, distributed FREE to members. This is also the official journal for some of our sister associations in Europe and of FELASA, the Federation of European Laboratory Animal Science Associations. The journal year runs from January to December during which time four issues are published; and (6) Membership discounts for Association meetings and events.

**REQUESTORS:** Laboratory animal users.

**COSTS:** Varies according to materials.

**Nederlandse Vereniging voor Proefdierkunde (NVP)**  
**Dutch Association for Laboratory Animal Science**

C/O Agricultural University Wageningen  
CKP, P.O. Box 8129, 6700 EV  
Wageningen, THE NETHERLANDS

**CONTACT:** F.A.R. van den Brock, Secretary

**TYPE OF ORGANIZATION:** Professional

**RESOURCES/SERVICES:** Co-sponsor of *Laboratory Animals: The International Journal of Laboratory Animal Science and Welfare*.

**Scandinavian Federation for Laboratory Animal Science**

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**CONTACT:** Barbro Salomonsson

**TYPE OF INSTITUTION/ORGANIZATION:** Professional

**RESOURCES:** Scand-LAS actively promotes: (1) the understanding of the need of animals in research, to the advantage of both other animals and man; (2) the welfare of laboratory animals; (3) the education of all personnel involved in the use of laboratory animals; (4) the dissemination of objective information concerned with use of laboratory animals; (5) the accreditation of laboratory animal facilities; (6) the accreditation of laboratory animal courses; and (7) working groups on selected issues. Scand-LAS is a member of the international laboratory animal science organization FELASA (Federation of the European Laboratory Animal Science Associations) and ICLAS (International Council for Laboratory Animals). Scand-LAS has standing working groups on education, health monitoring and pain, stress and discomfort, as well as policy. A meeting is held every Spring in connection with the general assembly. Following a fixed order, Denmark, Norway, Finland and Sweden are the host countries for these meetings.

Scand-LAS publishes a quarterly journal, *Scandinavian Journal of Laboratory Animal Science*, with papers on basic and applied laboratory animal science. The Journal also disseminates information and news of particular interest to members. The Journal is free to members of Scand-LAS. The Editorial Office is: Arne Rohmann, Skomagerkrogen 14, DK-4000 Roskilde, Denmark. Tel. +45 4635 3168. Fax +45 6525 3114. Email: [rrcons@image.dk](mailto:rrcons@image.dk)

**COSTS:** Journal subscriptions are priced for individual and library subscriptions. Membership dues are paid annually.



**Schweizerische Gesellschaft für Versuchstierkunde (SGV)  
Société Suisse pour la Science des Animaux de Laboratoire  
Swiss Laboratory Animal Science Association**

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4002 Basel SWITZERLAND

**CONTACT:** Dr. Dr. Brunhilde Illgen-Wilcke, Secretary

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**WORLD WIDE WEB:** <http://www.sgv.org>

**RESOURCES/SERVICES:** Several commissions support the board in the necessary scientific and educational activities and in the important field of laboratory animal protection. An informal Newsletter is published twice a year; the official journal of the society is *Laboratory Animal*. Every year a scientific meeting is organized, usually as a symposium at the annual meeting of the Swiss Union of Societies for Experimental Biology. A two-day training course or workshop on a selected topic is held in the autumn. Each year the society awards a prize to an outstanding contribution in the field of laboratory animals. Financial support may be granted to young researchers attending training courses or meetings. Eligible as ordinary members are persons who hold appropriate qualifications in biological, veterinary or medical sciences or who, by their experience and attainments, qualify as respected specialists in the field of laboratory animal science. Eligible as institutional members are persons or organizations intending to support the activities of the society.

**REQUESTOR:** Laboratory animal users.

**COSTS:** Vary according to material. Currently the membership fees are sfr 50.- for ordinary and sfr 300.- for institutional members.

**Sociedad Española para las Ciencias del Animal de Laboratorio  
Spanish Society for Laboratory Animal Science**

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**WORLD WIDE WEB:** <http://www.secal.es>

**CONTACT:** Secretaría

**TYPE OF INSTITUTION/ORGANIZATION:** Professional

**RESOURCES/SERVICES:** Established in 1989 to improve the care of laboratory animals used in human and animal health by bringing together laboratory animal professionals. SECAL holds Congresses and national and regional scientific meetings. SECAL has many publications available including Spanish translations of journal articles, guidelines, and policies.

**REQUESTOR:** Laboratory animal users.

**COSTS:** Vary according to materials or specific course.

## **Universities Federation for Animal Welfare**

The Old School  
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**WORLD WIDE WEB:** <http://www.users.dircon.co.uk/~ufaw3/#index>

**CONTACT:** James K Kirkwood BVSc PhD CBiol FIBiol MRCVS, Scientific Director

**TYPE OF INSTITUTION/ORGANIZATION:** Private, charitable

**RESOURCES/SERVICES:** Publishes *The UFAW Handbook on the Care and Use of Laboratory Animals*, a comprehensive guide to all laboratory species. Publications, reprints, videos, educational brochures, and advisory services. Publishes a quarterly scientific journal entitled *Animal Welfare*, which brings together scientific information from zoos, laboratories, farms, wildlife and companion animals.

**REQUESTOR:** Anyone.

**COSTS:** Vary according to materials. The annual membership fee for students and non-wage earners is £5 and for those in paid employment £10. Annual subscriptions to the journal *Animal Welfare* cost UFAW members £40/US\$80; individuals £50/US\$100; or libraries £70/US\$140.

## **Zentralstelle Zur Erfassung Und Bewertung von Ersatz Und Erganzungsmethoden Zum Tierversuch (Zebet)**

### **Center for Documentation and Evaluation of Alternative Methods to Animal Experiments**

Diedersdorfer Weg 1.

D-12277 Berlin, GERMANY

**TELEPHONE:** + 49 30 8412 2271

**FAX:** + 49 30 8412 2958

**E-MAIL:** [ZEBET@bgvv.de](mailto:ZEBET@bgvv.de)

**CONTACT:** Dr. Horst Spielmann or Dr. Barbara Grune

**TYPE OF INSTITUTION/ORGANIZATION:** Federal government

**RESOURCES/SERVICES:** Producer of the *ZEBET DATABANK AND INFORMATION SERVICE ON ALTERNATIVE METHODS TO ANIMAL EXPERIMENTS*. The ZEBET data bank contains documents on alternatives to the use of experimental animals, as presented in the international scientific literature. Each record contains a short description of a method in its most important details, i.e. aim, principle, and the stage of development or validation of the method and bibliographic references. An evaluation by ZEBET staff indicates whether the method results in the replacement, reduction or refinement of animal use according to the "3R's." Information is available on over 300 methods from the following subjects: pharmacology, toxicology, bacteriology, virology, food hygiene, parasitology, immunology, neurology, cancer research and animal production. The database contains a total of 4300 bibliographical references. Lists of methods, keywords and sources of literature are available.

ZEBET is a part of the Federal Institute for Health Protection of Consumers and Veterinary Medicine, Berlin. ZEBET is responsible for the documentation of alternative methods and also for

validation and acceptance of alternative methods at the national and international level, e.g. by the EU and OECD.

At present, requests for information have to be in the form of enquiries to ZEBET staff. ZEBET's staff are trained in the biomedical sciences, as well as in searching strategies for open access databank. An online connection to DIMDI, the German Institut for Medical Documentation and Information, provides direct access to all important national and international biomedical databases. The available information on a particular problem in the field of alternative methods is evaluated by ZEBET's staff and given to the user, including print-outs from the ZEBET databank, and references of the search in external databases. In controversial cases, ZEBET makes an official statement to the regional authorities which may be used in a court case. In addition, ZEBET handles more general queries on alternatives from all sectors of society.

**REQUESTOR:** Federal departments, federal authorities, local committees, animal welfare officers, scientists, research institutions, universities, manufacturing industry, animal welfare organizations, the interested public, and journalists.

**COSTS:** Contact the Center.

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## APPENDIX A

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THIS DOCUMENT IS INTENDED TO BE AN AID IN THE PREPARATION OF A DOD ANIMAL USE PROPOSAL. IT IS A COMPANION DOCUMENT TO AN IDENTICAL PROTOCOL FORMAT OR TEMPLATE THAT DOES NOT HAVE THE WRITTEN EXPLANATION FOR INDIVIDUAL PARAGRAPHS (See pages 14-18 of this document). THEY ARE DESIGNED TO BE USED ON A WORD PROCESSING PROGRAM, i.e., WordPerfect, WordStar, MicrosoftWord, WordPerfect for Macintosh, etc., SO THAT YOU ARE NOT LIMITED BY THE SPACE PROVIDED, AND SUGGESTED CHANGES OR MODIFICATIONS CAN BE QUICKLY AND EASILY MADE. USING A WORD PROCESSOR MAKES THIS FORMAT A "FILL-IN-THE-BLANKS" EXERCISE.

THE EXPLANATIONS OR INSTRUCTIONS MAY BE BLOCKED OUT AND DELETED IF IT IS MORE CONVENIENT TO USE THIS FORM RATHER THAN THE OUTLINE AVAILABLE WITHOUT THE EXPLANATIONS.

SPECIFIC RESPONSES REQUESTED IN THE FORMAT ARE A RESULT OF THE REQUIREMENTS OF THE ANIMAL WELFARE ACT (AWA), DOD REGULATIONS, OR ANIMAL WELFARE GUIDELINES. EACH PARAGRAPH SHOULD HAVE A RESPONSE. SOME PORTIONS OF THE PROTOCOL FORMAT MAY NOT BE APPLICABLE TO YOUR PARTICULAR PROTOCOL, i.e., NO SURGERY OR NO PROLONGED RESTRAINT. THESE SECTIONS SHOULD BE MARKED "N/A". THEY SHOULD NOT BE OMITTED.

IF SOPs OR OTHER DOCUMENTS ARE READILY AVAILABLE TO THE IACUC, THEY MAY BE REFERENCED TO ASSIST IN THE DESCRIPTION OF SPECIFIC PROCEDURES. IT IS CRITICAL THAT ONLY ANIMAL STUDIES OR PROCEDURES DOCUMENTED IN AN APPROVED PROTOCOL ARE PERFORMED IN THE ORGANIZATION. ADDITIONALLY, P.I.s OR OTHER ANIMAL USERS SHOULD KEEP ACCURATE EXPERIMENTAL RECORDS, AND BE ABLE TO PROVIDE AN AUDIT TRAIL OF THEIR ANIMAL EXPENDITURES AND USE THAT CORRELATES TO APPROVED PROTOCOLS.

\*\*\*\*\*



PROTOCOL NUMBER: \_\_\_\_\_

Received by LACUC \_\_\_\_\_

Approved/Sent for Revision \_\_\_\_\_

Received (2nd Time) by LACUC \_\_\_\_\_

Date Approved/Disapproved by LACUC \_\_\_\_\_

Previous Number \_\_\_\_\_

ACTIVE/COMPLETED/TERMINATED \_\_\_\_\_

PROTOCOL TITLE: \_\_\_\_\_

SHORT TITLE: \_\_\_\_\_

PRINCIPAL INVESTIGATOR \_\_\_\_\_ PI PHONE: \_\_\_\_\_  
(Print Rank, First & Last Name)

ASSOCIATE INVESTIGATOR \_\_\_\_\_  
(Print Rank, First & Last Name)

ASSOCIATE INVESTIGATOR \_\_\_\_\_  
(Print Rank, First & Last Name)

DEPARTMENT \_\_\_\_\_ DIVISION \_\_\_\_\_  
APC \_\_\_\_\_ RAD \_\_\_\_\_ STO \_\_\_\_\_ TASK \_\_\_\_\_ 1498 ASSN \_\_\_\_\_

ANIMAL REQUIREMENTS:

Species	Strain	Age	WT	Sex (M,F,E)	Total Number	Max no. housed

IS SPECIAL HOUSING REQUIRED? (YES/NO) If yes, explain or cite section in protocol: \_\_\_\_\_

ARE ANIMAL REQUIREMENTS RESTRICTED TO A SINGLE VENDOR? \_\_\_\_\_

ESTIMATED ANIMAL CARE COSTS (does not include other costs associated with protocol):

a. Cost of each animal \_\_\_\_\_ x number of animals required \_\_\_\_\_ = \_\_\_\_\_

b. Cost of per diem for animal species \_\_\_\_\_ x number of days on study \_\_\_\_\_ = \_\_\_\_\_

c. Total of a + b = \_\_\_\_\_

LITERATURE SEARCHES (for unnecessary duplication and 3Rs Alternatives) :

SEARCH TERMS \_\_\_\_\_

DATABASES SEARCHED: \_\_\_\_\_ DATE OF SEARCH(ES): \_\_\_\_\_

INDEX KEY WORDS (At least 5 words: e.g. species, strain, condition studied, studied): \_\_\_\_\_

BIOHAZARD and / or SAFETY ELEMENTS? Y/N REFERENCE PAGE IN PROTOCOL: \_\_\_\_\_

BIOSAFETY LEVEL: 1, 2, 3, 4 HAZARDS: a. Chemical b. Radiation c. Other (specify): \_\_\_\_\_

NAME of AGENT(S): \_\_\_\_\_

USDA CATEGORY

Number of Animals in Category  
Year 1 Year 2 Year 3

[ ] N - Minimal, Transient, or No Pain and Distress

[ ] D - Pain, Distress Relieved by Appropriate Measures

[ ] P - Unrelieved Pain or Distress

For P, ATTACH USDA FORM 18-23 and CITE REFERENCE PAGE IN PROTOCOL: \_\_\_\_\_

ALTERNATIVES CONSIDERATIONS: Does the protocol have any provisions that would qualify it to be identified as one that Refines, Reduces, or Replaces (3R's) the use of animals in relation to other protocols or procedures performed in the past?

YES/NO REFERENCE PAGE IN PROTOCOL: \_\_\_\_\_

**PROTOCOL SIGNATURE SHEET:** Requires one signature from the Primary Investigator; someone responsible for scientific review; an Attending Veterinarian; someone responsible for statistical review; and the Division's LACUC representative. Coordination signatures from any additional personnel providing support (Co-investigators, Coordinating Departments, IACUC Chair, Biosafety Review etc.) are highly recommended.

**PROTOCOL TITLE:**

**PRINCIPAL INVESTIGATOR:** \_\_\_\_\_

**SCIENTIFIC REVIEW:** Signature verifies that this proposed animal use protocol has received appropriate peer scientific review, and is consistent with good scientific research practice. (No response is required to the title paragraph of this section)

\_\_\_\_\_  
(Research Unit Chief/Directors signature)

**COORDINATION:** Name, signature, and date for the appropriate person or office are required. (No response is required to the title paragraph of this section)

**A. Attending/Consulting Veterinarian:** (Example) The attending/consulting veterinarian has reviewed the protocol and was consulted in the planning of procedures that require veterinary input, i.e., an unalleviated pain procedure. In addition, the veterinarian/veterinary medicine department has assisted with coordination for veterinary support to the protocol. (No response is required to the title paragraph of this section)

\_\_\_\_\_  
(Attending/Consulting Veterinarian)

**B. Statistician:** A person knowledgeable in statistics has reviewed the experimental design. (No response is required to the title paragraph of this section)

**C. LACUC Representative:** \_\_\_\_\_

**D. Other:** \_\_\_\_\_ You may wish to add specific additional offices or individuals for coordination purposes pertinent to your facility or operation.

(Start Separate Page)

**PROTOCOL TITLE:**

**PRINCIPAL INVESTIGATOR:**

**CO-INVESTIGATOR(S):**

**I. NON-TECHNICAL SYNOPSIS:** A brief, narrative description of the proposal or idea that is easily understood by non-scientists.

**II. BACKGROUND:**

**A. Background:** This should include a brief statement of the requirement or need for the information being sought. Lengthy explanations are not required. Typically, the "literature or the experience that led to the proposal will be briefly reviewed" (AR 70-18), and a description of the general approach should be provided. Unnecessary duplication of effort should be strictly avoided.

**B. Literature Search:** This search must be performed to prevent unnecessary duplication of previous experiments. DTIC is often required for DOD funded research. An additional search of the scientific literature (MEDLINE, GRATEFUL MED, MEDLARS, AWIC, etc.) is highly recommended.

**1. Literature Source(s) Searched:**

**2. Date and Number of Search:**

**3. Key Words of Search:**

**4. Results of Search:** Provide a narrative description of the results of the literature search(s).

**III. OBJECTIVE/HYPOTHESIS:** In non-technical terms, state the objective of this protocol, or the hypothesis to be accepted or rejected.

**IV. MILITARY RELEVANCE:** With regards to military needs and mission requirements, this paragraph should provide a brief and succinct military justification for the research. If applicable state the Science and Technology Objective (STO) that this work supports.

**V. MATERIALS AND METHODS:**

**A. Experimental Design and General Procedures:** Provide a complete description of the proposed use of animals. This section should succinctly outline the formal scientific plan and direction for experimentation. If several experiments or sequential studies are to be

included in the protocol, description of the experimental design for each separate experiment should be contained in sub-parts to this section. The length and detail required in this section depends largely on the complexity of the study. However, **a clearly understandable description of the numbers of animals and their distribution into experimental groups is essential.** The number requested should be the minimum numbers necessary to complete the study, but must be sufficient to yield meaningful results. If too few animals are requested and statistical significance is not achieved, the animals will have been misused. Be certain to include animals necessary for controls or technique development, etc. If the design is complex, a summary table or flow chart showing the distribution of animals by experimental group should be included. **The total number of animals required for the study is listed in section V.B.4. It is critical that reviewers of this protocol are able to follow your reasoning and calculations for the number of animals required, and can verify that the experimental design clearly supports the number of animals requested.**

1. Experiment 1:
2. Experiment 2: (etc.)

#### **B. Laboratory Animals Required and Justification:**

1. **Non-animal Alternatives Considered:** Were alternatives to animal use considered? **No study using animals should be considered prior to the elimination of all reasonable possibilities that the question might be adequately answered using other than animal means, i.e., computer modeling, cell cultures, etc.**

2. **Animal Model and Species Justification:** It is important that you adequately justify that animals are necessary for attainment of the research/training objectives. Moreover, justify the selection of this particular animal model. Investigators should use the least sentient species that will permit the attainment of research objectives. Why was this particular animal chosen? Were there other animal models considered that are lower on the phylogenetic scale (e.g., mice instead of rabbits)? Is there a unique quality or usefulness about this species that warrants its selection for use?

3. **Laboratory Animals:** No response necessary to the title paragraph of this section.

a. **Genus & Species:**

b. **Strain/Stock:** If inbred or specialized animals are required, please use proper terminology.

c. **Source/Vendor:** Provide a preferred source for the animals. Procurement of animals from non-USDA licensed sources requires an exception to policy. Enter the source/vendors USDA license number if available.



d. Age:

e. Weight:

f. Sex:

g. Special Considerations: Specialized requirements for the research animals should be reflected here, i.e., SIV or herpes antibody free, Pasteurella free, etc.

h. Other:

4. Total Number of Animals Required:

(a) mice            320 (example)

All that is required in this section is the total number of animals to be used on the study. The number requested here should match exactly those described in para V. A. , Experimental Design & General Procedures in the MATERIALS AND METHODS section. Keep in mind the number requested should be the minimum numbers necessary to complete the study, but must be sufficient to yield meaningful results. If too few animals are requested and statistical significance is not achieved, the animals will have been misused. Be certain to include animals necessary for controls or technique development, etc. If additional animals are needed due to technical or unavoidable circumstances, or to exploit a serendipitous finding, follow IACUC procedures for requesting approval for additional animals.

5. Refinement, Reduction, Replacement: The DoD must provide specific examples of its alternatives initiatives in the annual report to Congress. Does this protocol have any provisions that would qualify it to be identified as one that refines, reduces or replaces (3 R's) the use of animals? For example, does your study use statistical tests that require fewer animals, i.e., a modified LD50 test like Thompson & Weil, or are you using cell cultures, computer modeling or any other technique that will influence the numbers of animals required? Are you using animals lower on the phylogenetic scale? Please provide a short description of the features that you feel qualify the study as one that employs one of the "3 R's," or give a negative reply. No response is needed under the title paragraph of this section. **This information should be captured in such a way that it can be included in the DoD annual report submission.**

a. Refinement: The use of analgesia, or the use of remote telemetry to increase the quality and quantity of data gathered or adjusted early endpoint for the animals are examples of refinements.

b. Reduction: Use of shared control groups, preliminary screening in non-animal systems or innovative statistical packages are examples of reductions.

c. **Replacement**: Non-animal systems that eliminate the use of animals are examples of replacement.

**C. Technical Methods**: These should be presented in sufficient detail, documented or referenced, so that the IACUC can adequately review the procedure and obtain a clear understanding of what is to be done, how the animal will be handled, and make a reasonable determination as to whether this proposed use of laboratory animals is in compliance with DoD regulations, guidelines, and federal law. No response is needed under the title paragraph of this section.

1. **Prolonged Restraint**: Describe and justify in detail any prolonged restraint (greater than three hours) intended for use during the study, e.g., primate chairs, restraint boards, metabolism cages, etc. Also describe habituation procedures for the prolonged restraint. This section is not intended for short-term actions such as rabbit restraint for bleeding, etc. If there is prolonged restraint involved, who will be restraining the animals, and for how long?

2. **Surgery**: Major operative procedures on non-rodent species, i.e., rabbits, monkeys, etc., should be conducted only in dedicated facilities intended for that purpose, and operated and maintained under aseptic conditions. Non-major operative procedures & all rodent surgery do not require a dedicated facility, but must be performed using aseptic technique, i.e., surgical gloves, mask, sterile instruments. A major operative procedure is one that "penetrates and exposes a body cavity, or causes permanent impairment of physical or physiological function." The animal care unit personnel should assist in defining the requirements of this portion of the law if necessary. No response required under the title paragraph of this section.

a. **Procedure**: Describe in detail any surgical procedures planned.

b. **Pre- and Postoperative Provisions**: Detail the provisions for both pre- and postoperative care, including provisions for post-surgical observations. Also include the provider of that care, and the location for the postoperative care.

c. **Location**: Give the location\room # for the proposed surgical procedure.

d. **Multiple Survival Surgery Procedures**: If multiple major operative procedures on the same animal are intended, they must be adequately justified for scientific reasons by the P.I. in writing.

(1) **Procedures**:

(2) **Scientific Justification**:

3. **Animal Manipulations**: Any injections, sampling procedures, or other

manipulations of the animals necessary for the execution of the study must be described if not listed in section V. List needle sizes, routes of injection or withdrawal and anatomical location, e.g. 21 ga needle, SQ, IM, femoral vein, jugular vein etc., or the proposed method so that a reasonable evaluation of the appropriateness of the procedure can be made. You may furnish the committee a reference or SOP to document a particular procedure in lieu of a detailed description. You may wish to rearrange the subparagraphs of this section to suit your protocol. No response is needed under the title paragraph of this section.

a. **Injections**: There is no need to duplicate specific information already provided in section V.C.1.b., the Pain Alleviation, anesthesia/analgesia section of the proposal.

b. **Biosamples**: Cerebral taps, blood sampling, etc. List amounts taken and method for sampling. Procedures performed or biosamples obtained during a necropsy need not be described here.

c. **Animal Identification**: Microchip, tattoo, ear tags, cage cards, etc.

d. **Behavioral Studies**: Fully describe any intent to use aversive stimuli, food or water deprivation, etc, that would impact upon the animals in this study.

e. **Other procedures**: EKG's, radiology, aerosol exposure, etc.

4. **Adjuvants**: List any adjuvants and your plan for their use. Provide dosages & route.

5. **Study Endpoint**: What is the projected end point or termination of the study for the animals? Is death, euthanasia, or recovery expected; and what is the specific plan for determining when the animal experimentation phase will be stopped? You should ensure that unnecessary pain or distress is prevented by carefully considering "When is the experimental question answered?" so that the animals can be removed from the study as soon as feasible. Explain the plan for the disposition of surviving animals. **You must specifically address and justify any proposed use of death as an endpoint.**

6. **Euthanasia**: Explain the plan for euthanasia of the animals at the completion of the study and who will perform the procedure. The AWA defines euthanasia as "humane destruction of an animal by a method that produces rapid unconsciousness and subsequent death without evidence of pain or distress, or a method that utilizes anesthesia produced by an agent that causes painless loss of consciousness and subsequent death." The current AVMA guidelines for euthanasia must be followed. Exceptions to the AVMA guidelines will be considered by the IACUC on a case-by-case basis. Exceptions must be scientifically justified by the P.I. in writing. The attending veterinarian will assist in selecting the best method for euthanasia if requested.

7. **Pain**: The law defines a painful procedure as one that would "reasonably

be expected to cause more than slight or momentary pain or distress in a human being to which that procedure was applied, that is, pain in excess of that caused by injections or other minor procedures." **If a procedure involves pain or distress, the P.I. must consult with the attending veterinarian.** Respond N/A if the animals will experience "no pain or distress."

**a. USDA (Form 18-3) Pain category:**

This information is reported by the organization to the USDA on USDA Form VS 18-23. **The P.I. or primary user should estimate the number of animals that will be counted in each pain category.** If more than one species is requested in the proposal, reflect those animals in a duplicate table in this paragraph. **The total numbers reflected in these three categories should add up to the number and percent of animals requested for the entire protocol in para V.B.4.**

**(1) No Pain** \_\_\_\_\_(##)\_\_\_\_\_ % (Column C)

Studies involving no pain or distress beyond that expected on a momentary nature such as would occur with an injection, a deep palpation, grooming activities, etc.

**(2) Alleviated Pain** \_\_\_\_\_(##)\_\_\_\_\_ % (Column D)

Procedures wherein anesthesia or analgesia will be administered to avoid or alleviate pain or distress. General anesthesia given for surgical preparations, or the use of analgesia or anti-inflammatories would be examples for this category.

**(3) Unalleviated Pain or Distress** \_\_\_\_\_(##)\_\_\_\_\_ % (Column E)

Procedures where alleviation of pain or distress are contraindicated for some justifiable reason such as; would confound the experimental results if drugs relieving pain were administered. Detailed justification for putting animals into this category is required below in para V.C.1.d.

**b. Pain Alleviation:** The attending veterinarian should be able to provide assistance in completing this section of the proposal.

**(1) Anesthesia/Analgesia/Tranquilization:** Describe the methods or strategies planned to alleviate pain or distress. If pain alleviation is planned, specify who will be administering the analgesics, anesthetics, or tranquilizers during the study. Provide agent, dosage, route & site, indication, needle size, etc.

**(2) Paralytics:** No use of paralytic agents without anesthesia is allowed unless scientifically justified by the P.I. and approved by the IACUC.

**c. Alternatives to Painful Procedures:**

**(1) Source(s) Searched:** e.g., AWIC, AGRICOLA, CAAT, MEDLINE, etc.



(2) **Date of Search:**

(3) **Key Words of Search:** e.g. Pain, surgery,

(4) **Results of Search:** Provide a narrative description of the results of the alternatives literature search. "Research facilities will be held responsible, if it is subsequently determined that an alternative to a painful procedure was available to accomplish the objectives of the proposed experiment." The Animal Welfare Act specifically states that the **"P.I. must provide a narrative description of the methods and sources, e.g., the Animal Welfare Information Center, MEDLINE, LIFE SCIENCES ABSTRACTS, AGRICOLA, AND BIOSIS that he/she used to determine that alternatives to the painful procedure were not available."** It is a requirement to perform the alternatives literature search and painful procedure justification even when animals are placed in the alleviated pain category (column D).

**d. Painful Procedure Justification:** Procedures causing more than transient or slight pain that are unalleviated, must be justified on a scientific basis in writing by the P.I. The pain must continue for only the necessary period of time dictated by the experiment, and then be alleviated, or the animal humanely euthanized. This paragraph must be completed if there are any animals listed in either the alleviated (column D) or the unalleviated pain or distress (column E) category in para V.C.1. **The P.I. must consult with the attending veterinarian or his or her designee in the planning of both alleviated and unalleviated painful procedures, and state it here.**

**D. Veterinary Care:** Attending veterinary care of lab animals receives particular emphasis in the AWA. The attending veterinarian of your facility will assist P.I.s with preparing this section if requested. No response is necessary to the title paragraph of this subsection.

**1. Husbandry Considerations:** The law specifically states that animal housing and living conditions must be appropriate to their species, and contribute to their health and comfort. Describe husbandry or refer to SOP. If known, list the location the animals will be routinely housed and the length of housing requirement. Personnel in the animal care unit should be able assist P.I.s in the preparation of the protocol sections dealing with animal care issues.

**a. Study Room:** If stay exceeds 12 hours.

**b. Special Husbandry Provisions:** Micro-isolators, metabolic cages, etc.

**2. Attending Veterinary Care:** Will the animals be observed daily or more frequently, and by whom? What is the plan if the animal becomes ill or debilitated during the

study and requires supportive therapy? Will the animal be euthanized if it becomes critically ill or comatose, and by whom (study end point adjustment)? Justification for not providing supportive care for clinically ill animals is necessary.

**3. Enrichment Strategy:** Written justification for restricting enrichment programs or activity programs of dogs, cats, or nonhuman primates must be provided.

**a. Dogs:** Do you have any reason to restrict activity programs for dogs on this protocol that might be implemented by the animal care unit to comply with federal welfare regulations. If yes, justify.

**b. Nonhuman Primates:** Do you have any reason to prohibit environmental enrichment or enhancement strategies that might be implemented by the animal care unit to comply with federal welfare regulations. If yes, justify.

**E. Data Analysis:** List the statistical test(s) planned or the strategy intended to evaluate the data.

**F. Investigator & Technician Qualifications/Training:** List those animal procedures or manipulations described in the protocol that will be performed by each investigator or technician, and their training or qualifications to perform these procedures. Personnel conducting the "hands-on" animal procedures described in the protocol must be identified and appropriately trained and qualified to perform that procedure. **This is NOT questioning the P.I.'s PROFESSIONAL qualifications to conduct the research, but rather a requirement that personnel actually performing the research animal manipulations are technically competent, and thus are not inflicting unnecessary pain, distress, or injury to an experimental animal due to inexperience or improper technique.** Contact your attending veterinarian for assistance with this requirement.

**VI. Biohazard/Safety:** Provide a list of any potential biohazards associated with this proposal, e.g., viral agents, toxins, radioisotopes, oncogenic viruses, chemical carcinogens, etc. Explain any safety precautions or programs designed to protect personnel from biohazards, and any surveillance procedures in place to monitor potential exposures.

**(START NEW PAGE HERE)**

**VIII. ASSURANCES:** The law specifically requires several written assurances from the P.I. It states that "research facilities will be held responsible if it is subsequently determined that an experiment is unnecessarily duplicative, and that a good faith review of available sources would have indicated as much."

(This section will state) As the Primary Investigator on this protocol I acknowledge my responsibilities and provide assurances for the following:

**A. Animal Use:** The animals authorized for use in this protocol will be used only in the

activities and in the manner described herein, unless a deviation is specifically approved by the IACUC.

**B. Duplication of Effort:** I have made a reasonable, good faith effort to ensure that this protocol is not an unnecessary duplication of previous experiments.

**C. Statistical Assurance:** I assure that I have consulted with an individual who is qualified to evaluate the statistical design or strategy of this proposal, and that the "minimum number of animals needed for scientific validity are used."

**D. Biohazard\Safety:** I have taken into consideration, and I have made the proper coordinations regarding all applicable rules and regulations regarding radiation protection, biosafety, recombinant issues, etc., in the preparation of this protocol.

**E. Training:** I verify that the personnel performing the animal procedures/manipulations described in this protocol are technically competent and have been properly trained to ensure that no unnecessary pain or distress will be caused as a result of the procedures/manipulations.

**F. Responsibility:** I acknowledge the inherent moral and administrative obligations associated with the performance of this animal use protocol, and I assure that all individuals associated with this project will demonstrate a concern for the health, comfort, welfare, and well-being of the research animals. Additionally, I pledge to conduct this study in the spirit of the fourth "R" which the DoD has embraced, namely, "Responsibility" for implementing animal use alternatives where feasible, and conducting humane and lawful research.

---

(P.I. Signature)

**G. Painful Procedures:** (Include only if conducting research that will cause more than slight or momentary pain or distress (Column D or E by USDA classification) the following statement must follow.) **I am conducting biomedical experiments which may potentially cause more than momentary or slight pain or distress to animals that WILL BE relieved or WILL NOT (circle one) be relieved with the use of anesthetics, analgesics and/or tranquilizers.** I have considered alternatives to such procedures; however, using the methods and sources described in the protocol, I have determined that alternative procedures are not available to accomplish the objectives of the proposed experiment.

---

(P.I. signature)

**IX. Enclosures:** (Available for the attachment of the results of any literature searches, SOPs, references, or other documents pertinent to the protocol that you may wish to include. Local IACUC's should determine specific items to be included here.)

PROTOCOL TEMPLATE/OUTLINE without instructions

PAGE 1 IS THE PROTOCOL COVER SHEET (page 2 of this document)

START A NEW PAGE FOR THE SIGNATURE PAGE BELOW -

PROTOCOL TITLE:

PRINCIPAL INVESTIGATOR:

\_\_\_\_\_  
(Signature)

SCIENTIFIC REVIEW: (Research Unit Chief/Directors)

\_\_\_\_\_  
(Signature)

COORDINATION: (Optional)

A. Attending/Consulting Veterinarian:

\_\_\_\_\_  
(Signature)

B. Statistician:

\_\_\_\_\_  
(Signature)

C. Other:\_\_\_\_\_

START A NEW PAGE FOR BODY OF PROTOCOL

PROTOCOL TITLE:

PRINCIPAL INVESTIGATOR:

CO-INVESTIGATOR(S):

I. NON-TECHNICAL SYNOPSIS:

II. BACKGROUND:

A. Background:



B. Literature Search:

1. Literature Source(s) Searched:

2. Date and Number of Search:

3. Key Words of Search:

4. Results of Search:

III. OBJECTIVE\HYPOTHESIS:

IV. MILITARY RELEVANCE:

V. MATERIALS AND METHODS:

A. Experimental Design and General Procedures:

B. Laboratory Animals Required and Justification:

1. Non-animal Alternatives Considered:

2. Animal Model and Species Justification:

3. Laboratory Animals:

a. Genus & Species:

b. Strain/Stock:

c. Source/Vendor:

d. Age:

e. Weight:

f. Sex:

g. Special Considerations:

h. Other:

4. Total Number of Animals Required:

5. Refinement, Reduction, Replacement:

a. Refinement:

b. Reduction:

c. Replacement:

C. Technical Methods:

1. Prolonged Restraint:

2. Surgery:

a. Procedure:

b. Pre- and Postoperative Provisions:

c. Location:

d. Multiple Survival Surgery Procedures:

(1) Procedures:

(2) Scientific Justification:

3. Animal Manipulations:

a. Injections:

b. Biosamples:

c. Animal Identification:

d. Behavioral Studies:

e. Other procedures:

4. Adjuvants:

5. Study Endpoint:

6. Euthanasia:

7. Pain:

a. USDA (Form 18-3) Pain category:

(1) No Pain \_\_\_\_\_ (#) \_\_\_\_\_ % (Column C)

(2) Alleviated Pain \_\_\_\_\_ (#) \_\_\_\_\_ % (Column D)

(3) Unalleviated Pain or Distress \_\_\_\_\_ (#) \_\_\_\_\_ %  
(Column E)

b. Pain Alleviation:

(1) Anesthesia/Analgesia/Tranquilization:

(2) Paralytics:

c. Alternatives to Painful Procedures:

(1) Source(s) Searched:

(2) Date of Search:

(3) Key Words of Search:

(4) Results of Search:

d. Painful Procedure Justification:

D. Veterinary Care:

1. Husbandry Considerations:

a. Study Room:

b. Special Husbandry Provisions:

2. Attending Veterinary Care:

3. Enrichment Strategy:

a. Dogs:

b. Nonhuman Primates:

E. Data Analysis:

F. Investigator & Technician Qualifications/Training:

VI. Biohazard/Safety:

(Start new page here)

**VIII. ASSURANCES:** As the Primary Investigator on this protocol I provide the following assurances:

**A. Animal Use:** The animals authorized for use in this protocol will be used only in the activities and in the manner described herein, unless a deviation is specifically approved by the IACUC.

**B. Duplication of Effort:** I have made a reasonable, good faith effort to ensure that this protocol is not an unnecessary duplication of previous experiments.

**C. Statistical Assurance:** I assure that I have consulted with an individual who is qualified to evaluate the statistical design or strategy of this proposal, and that the "minimum number of animals needed for scientific validity are used."

**D. Biohazard\Safety:** I have taken into consideration, and I have made the proper coordinations regarding all applicable rules and regulations regarding radiation protection, biosafety, recombinant issues, etc., in the preparation of this protocol.

**E. Training:** I verify that the personnel performing the animal procedures/manipulations described in this protocol are technically competent and have been properly trained to ensure that no unnecessary pain or distress will be caused as a result of the procedures/manipulations.

**F. Responsibility:** I acknowledge the inherent moral and administrative obligations associated with the performance of this animal use protocol, and I assure that all individuals associated with this project will demonstrate a concern for the health, comfort, welfare, and well-being of the research animals. Additionally, I pledge to conduct this study in the spirit of the fourth "R" which the DoD has embraced, namely, "Responsibility" for implementing animal use alternatives where feasible, and conducting humane and lawful research.

---

(P.I. Signature)

**G. Painful Procedures:** (Include above if conducting research that will cause more than slight or momentary pain or distress (Column D or E by USDA classification) the following statement must follow.) **I am conducting biomedical experiments which may potentially cause more than momentary or slight pain or distress to animals that WILL BE relieved or WILL NOT (circle one) be relieved with the use of anesthetics, analgesics and/or tranquilizers.** I have considered alternatives to such procedures; however, using the methods and sources described in the protocol, I have determined that alternative procedures are not available to accomplish the objectives of the proposed experiment.

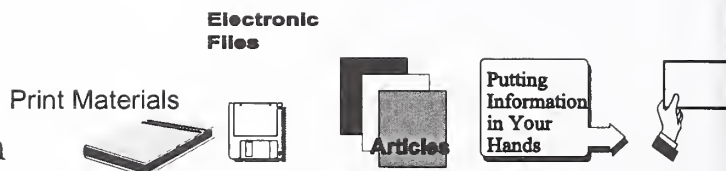
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(P.I. Signature)

**IX. Enclosures:** (Available for the attachment of the results of any literature searches, SOPs, references, or other documents pertinent to the protocol that you may wish to include. Local IACUC's should determine specific items to be included here.)



# National Agricultural Library Document Delivery Services Branch



## Services Available to Individuals

The National Agricultural Library (NAL) supplies agricultural materials not found elsewhere to other libraries and information centers. Submit requests **first to your local library resources**. In the United States, possible sources are public libraries, state libraries, land-grant university or other large research libraries within a state. In other countries submit requests through major university, national, or provincial institutions.

If the publications are not available from your local library, **have your library submit requests to NAL** with a statement indicating their non-availability following the directions below.

### Library Must Include the Following Data Elements in Each Request:

- Complete mailing address. (Library's Fax number or ARIEL™ IP address, if delivery by either of these methods is desired).
- Complete citation including verification (source of citation) and NAL call number if available.
- Date after which item is no longer needed.
- Copyright Compliance -- Libraries may indicate compliance by including the initials of one statement, either "CCL" for compliance with the copyright law or "CCG" for compliance with Copyright Guidelines or a statement that the request complies with U.S. Copyright Law or other acceptable copyright laws (i.e. IFLA, CLA, etc.). Libraries must also provide authorizing official's name.
- Willingness to pay charges must be indicated on the form.

The library must submit a separate interlibrary loan form or request for each item. If the citation is from an NAL database (AGRICOLA, *Bibliography of Agriculture*, or the NAL Catalog) and the call number is given, please include it. Materials in NAL's collection are loaned only to other U.S. and Canadian libraries. The following materials are not loaned: serials, rare materials, reference and reserve books, microforms, and proceedings of conferences or symposia. Photocopy or microform of non-circulating publications may be requested for a fee provided that the request does not exceed 50 pages per item.

### Send Requests to:

**Postal Mail:** USDA, National Agricultural Library  
Document Delivery Services Branch, PhotoLab  
10301 Baltimore Ave., NAL Bldg.  
Beltsville, Maryland 20705-2351

**FAX:** 301-504-5675  
**Ariel IP Address:** ariel.nal.usda.gov  
**E-mail:** lending@nal.usda.gov  
**OCLC:** AGL

### Charges for delivery:

- Photocopy, hard copy of microfilm and microfiche -- \$5.00 for the first 10 pages or fraction copied from a single article or publication. \$3.00 for each additional 10 pages or fraction.
- Duplication of NAL-owned microfilm -- \$10.00 per reel.
- Duplication of NAL-owned microfiche -- \$5.00 for the first fiche and \$.50 for each additional fiche per title.

**Billing** -- Charges include postage and handling, and are subject to change. Invoices are issued quarterly by the National Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, VA 22161. Establishing a deposit account with NTIS is encouraged. **DO NOT SEND PREPAYMENT.**

Contact the Access Services Librarian at (301) 504-6503 or via email at [access@nal.usda.gov](mailto:access@nal.usda.gov) with questions or comments about this policy.

# National Agricultural Library Document Delivery Services Branch

Print Materials

Electronic  
Files

Articles

Putting  
Information  
in Your  
Hands

## Services Available to Libraries, Institutions and Organizations

The National Agricultural Library (NAL) accepts requests from libraries and other organizations in accordance with the national and international interlibrary loan code and guidelines. In its national role, NAL supplies copies of agricultural materials not found elsewhere. Submit requests to major university libraries, national or provincial institutions or network sources prior to sending requests to NAL. If the needed publications are not available from these sources, submit requests to NAL with a statement indicating their non-availability.

**Materials in NAL's collection are not loaned outside the United States; however, copies of materials may be provided.** There is a limit of 50 pages per item to comply with copyright law.

**AGLINET** -- Requestors in countries with an AGLINET library are encouraged to make full use of that library and its networking capabilities. As an AGLINET participant, NAL provides free document delivery service for materials published in the United States to other AGLINET participants.

**Requests** -- Submit requests on the American Library Association (ALA) or the International Federation of Library Associations and Institutions (IFLA) interlibrary loan form, or via electronic mail, Ariel™, or facsimile. (See further details under *For Electronic Access and Delivery* below.)

### Charges:

- Photocopy, hard copy of microfilm and microfiche--\$5.00 for the first 10 pages or fraction copied from a single article or publication. \$3.00 for each additional 10 pages or fraction.
- Duplication of NAL-owned microfilm--\$10.00 per reel.
- Duplication of NAL-owned microfiche--\$5.00 for the first fiche and \$.50 for each additional fiche per title.

**Billing** -- Charges include postage and handling, and are subject to change. Invoices are issued quarterly by the National Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, VA 22161. Establishing deposit accounts with NTIS is encouraged. Annual billing is available on request by contacting NAL at the address below. **DO NOT SEND PREPAYMENT.**

### For postal service delivery send requests to:

USDA National Agricultural Library  
Document Delivery Services Branch  
4th Floor PhotoLab  
10301 Baltimore Ave., NAL Bldg.  
Beltsville, Maryland 20705-2351

### For electronic access and delivery :

The Document Delivery Services Branch accepts ILL requests from libraries via several electronic methods. All requests must comply with established routing and referral policies and procedures. A sample format for ILL requests follows.

**INTERNET**.....lending@nal.usda.gov  
Start the subject line with one word format:

3 letter month abbreviation + day + NAL + # of request placed that day,  
*For Example:* jul25NAL4 (if this is the fourth request on July 25).  
*For Example:* jul 25NAL1-4 (if this is four requests submitted at one time)

**OCLC**.....AGL

**TELEFACSIMILE**.....301-504-5675

Requests can be created on standard ILL forms and then faxed. NAL will fill via FAX at no additional cost if FAX number is included on request. NAL will send up to 30 pages per article. If request exceeds 30 pages, NAL will ship via postal service. There is no RUSH service.

**ARIEL™ .....198.202.222.162**

NAL will fill the request via ARIEL™ if the ARIEL™ address is included in the request. NAL treats ARIEL™ as an alternative delivery mechanism--not an expedited service. NAL will send up to 30 pages per article via ARIEL™. If request exceeds 30 pages, NAL will ship via postal service.

### **Required data elements for all requests:**

- Complete mailing information for all requests regardless of method of delivery. (Borrower's Fax number or ARIEL™ IP address if delivery by either of these methods is desired.)
- Complete citation including verification (source of citation) and NAL call number if available.
- Date after which item is no longer needed.
- Copyright Compliance -- Pre-printed forms must contain your signature to indicate copyright compliance. On e-mail requests include the complete Statement of Copyright Compliance. Libraries may indicate compliance by including the initials of one statement, either "CCL" for compliance with the copyright law or "CCG" for compliance with Copyright Guidelines or a statement that the request complies with U.S. Copyright Law or other acceptable copyright laws (i.e. IFLA, CLA, etc.). Libraries must also provide authorizing official's name. Requests will be rejected if this information is not included.
- Maximum cost you are willing to pay for billing purposes.

### **Sample Electronic Mail Request**

(Your Institutions Name)/NAL JUL25NAL1 Date Not Needed After: 9/25/97

(Your Department or Office  
Your University Library or Institution  
City, State or Province, Country, Mail Code)

Dr. Smith (patron name) Biology Dept. (patron office)  
Canadian Journal of Soil Science 1988 v 68(1): 17-27 (complete citation)  
De Jong, R. Comparison of two soil-water models under semi-arid growing conditions

**NAL Call Number:** 56.8 C162 **Ver:** AGRICOLA

**Remarks:** Not available at university or in region

**Authorized by:** Charles Johnson

CCL

**Maxcost:** \$15.00

(your) Phone# (301)555-1234

(your) Fax#: (301)555-5678

(your) ARIEL IP Address: 111.222.333.444.555

Contact the Access Services Librarian, Document Delivery Services Branch at (301) 504-6503 or via Internet at [access@nal.usda.gov](mailto:access@nal.usda.gov) with questions or comments about this policy.

NATIONAL AGRICULTURAL LIBRARY



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